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NORMAL BONE, DISEASED BONE, DEAD BONE

CALDWELL LECTURE, 1953*

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INTRODUCTION

LIKE all Caldwell lecturers faced with the responsibility of preparing to talk for an hour to a captive audience of radiologists, I have had to choose between two general courses that were open to me. I might aspire to something like a complete treatment of a narrow field or might deal with a wider field in a manner far from complete. I have elected to deal lightly and most incompletely with a wide field, giving some of its historical background and a few bits of its technical details, and the field I have chosen is "skeletal tissue—its nature during health and the changes that come with disease and death."

In the years since 1920, thirty-one lecturers have honored the memory of Eugene Caldwell (1870–1918) by addressing this Society on some subject related to Radiology, but of all these only Neuhauser[27] has dealt primarily with the roentgenology of the skeleton. This fact would have seemed strange to Caldwell because in his day the diagnosis of diseases and injuries of bone constituted the most common task of the radiologist whereas examination of the lungs, alimentary tract, urinary tract, etc., was only beginning to become important. We have been using roentgen rays to examine bones ever since Röntgen (1845–1923) himself showed the way by making a plate of the hand of his anatomical colleague, von Kölliker (1817–1905), and though in this fifty-eighth year of the existence of our specialty we radiologists may justly claim to know a great deal about the growth, disease and death of bone, still we must admit that there is much we do not know.

Human and animal skeletons have been plentifully available throughout the centuries for study by professional and amateur anatomists and pathologists, and by means of fossils such studies have been carried back to prehistoric times. Before the days of the microtome, bone and cartilage were easier to slice than the soft tissues, and even with the crude microscopes of the seventeenth and eighteenth centuries many of the details of osseous histology were worked out, but paradox-

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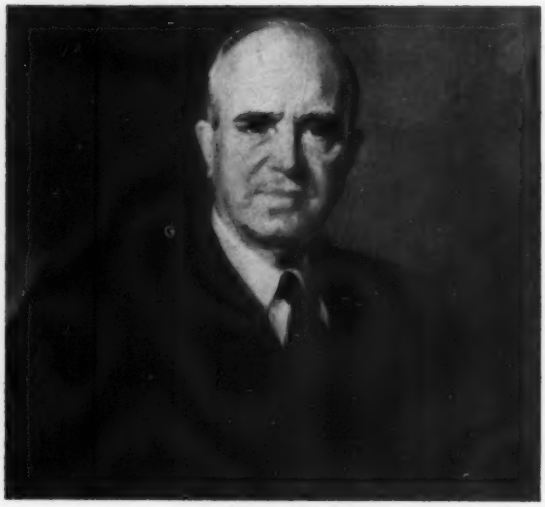

FIG. 1. Dallas Burton Phemister, M.D. Born July 15, 1882, died December 28, 1951. Chairman, Department of Surgery, University of Chicago, 1927–1947. (From portrait by Edmund Giesbert.)

ically the hardness of bone which had been advantageous previously became a nuisance once techniques had been developed for embedding and sectioning soft tissues. All modern pathologists are equipped to decalcify, embed and section small pieces of bone, but in only a few laboratories are there facilities for making large sections, such as, for example, of the entire knee joint. Even in such laboratories the development of bone pathology is hampered by the fact that many weeks must elapse between the time surgery is performed and the time when the decalcified stained and mounted sections are available for study. Once such sections are available, they are adequate for the needs of the pathologist, decalcification per se not being disadvantageous, but in some phases of experimental work it is necessary to work with nondecalcified bone. McLean, Bloom, Urist and their associates have perfected techniques for sectioning undecalcified bone that are practical with the growing bones of young rats and the earlier stages of callus in repairing fractures of large animals and man.

If he were alive, my friend, teacher and colleague, Dallas B. Phemister (1882–1951), would have been the proper person to address you on this subject, and if I am able to hold your attention for this hour it will be largely because of what I have learned directly from him or from others whose work has been influenced by his teaching (Fig. 1). Dr. Phemister was not only an experienced and skillful surgeon but also a physiologist, pathologist and, above everything else, an inspired teacher. He became known first for his work in bone pathology and throughout his life continued to practice orthopedic surgery and study skeletal disease, but his contributions were not limited to orthopedics or even to surgery. He examined the role of external and interstitial hemorrhage in shock, contributing important links in the knowledge that led to the present-day, large-scale employment of blood transfusions. He investigated the relationship between occlusion of the cystic duct and the deposition of calcium in the gallbladder and took a prominent part in developing modern surgical procedures for dealing with carcinoma of the esophagus. Those of us who were close to him believe that Dr. Phemister's greatest single contribution to American medicine was the example he set for the scores of undergraduate and graduate students who worked with him during the quarter century of his service at The University of Chicago; but if he is remembered by medical historians, probably it will be for his publications on necrosis of bone. Some of the slides that I will show are from the collection that was started by Dr. Phemister and for many years past has been in the process of being reorganized, reclassified and greatly enlarged by his student and colleague, Howard Hatcher. For the unearthing of seventeenth, eighteenth and nineteenth century sources I am indebted to the skill and diligence of Mrs. George Gomori, our medical librarian; and for access to original publications or microfilms of them my thanks are due to General DeCoursey of the Armed Forces Institute of Pathology and to the custodians of the libraries of the Surgeon General, of North-

western University Medical School, and of The University of Chicago.

LIVE BONE

The fact that bone is living tissue must have been appreciated for as long as man has been concerned with the structure and function of his own body and the bodies of the game or domestic animals on which he subsists. Even primitive man must have known that bone grew as the body grew, was soft in very young animals and hard in those that were fully grown. He saw bone bleed when it was exposed to view in compound fractures and he knew that sometimes limbs broken in accidents mended so that function was restored. The surgeons of ancient Egypt and Greece and of medieval Europe knew something of the gross anatomy of the skeleton and were experienced in the treatment of fractures and the performing of amputations, but it was not until the close of the seventeenth century that the histology of bone began to evolve. Clopton Havers, M.D. (1650–1702), citizen of London and a Fellow of the Royal Society, was an important contributor during this period, but not all his views seem as sound to us today as those concerning the organization of bone cells into what are now termed "haversian systems" in honor of him. For example, in his "Osteologia Nova," published in 1691, Havers[15] says of the periosteum: "I come now to consider the Design and Use of the Periosteum and first it is to be a Tegument to the Bones; for Nature in the Formation of all of the parts is found to be Elegant as well as Provident and though it could be granted that the Membrane serves no necessary Use, yet it is for Decency." It soon became known, however, that the periosteum had uses other than the cloaking of the nakedness of bone. Mr. W. Cheselden (1688–1752), surgeon to His Majesty's Royal Hospital at Chelsea and the author of "Anatomy of the Human Body" which for may years was the standard text for English medical students, in the year 1712 described the periosteum as a membrane which carried the vascular network that supplies blood to the nutrient vessels of the bone, a concept which seems safe for all time. But though Cheselden had this sound concept of skeletal vascularization, he did not appreciate the bone-building attributes of periosteum and thought of the bones as possessing some sort of ossifying juice. Of this he says:[9] "Sometimes the ossifying matter flows out of the bones and forms bony excrescences and frequently in old men it fixes on the arteries and makes them grow bony."

It was not until the summer of 1736 that a chance observation by a young London surgeon, John B. Belchier (1706–1785), set off a train of events that greatly accelerated the progress of skeletal physiology. He noted that certain cooked pork that was served to him was of normal taste and normal appearance except for the fact that the bones were stained red. On investigation he found that the pork was from pigs whose usual diet had been augmented by bran that had been used to adsorb excess color from freshly dyed calicoes. Some of the dyes that had been used contained iron, others lead; but since madder was a common ingredient to all of them, he assumed that madder was the factor that reddened the bones of the pigs. Experiments proved the soundness of his guess because chickens, whose normal diet was fig dust, on having madder added to that feed promptly developed a redness of bones which did not fade with boiling or on extraction with alcohol. Belchier, who was on the staff of Guy's Hospital and a Fellow of the Royal Society, reported his findings to that society and published two papers in the *Philosophical Transactions* of 1735 and 1736, vol. 39, the first being entitled, "An Account of the Bones of Animals Being Changed to a Red Color by Aliment Alone,"[4] the second, "A Further Account of the Bones of Animals Being Made Red by Aliment Alone."[5] To John Belchier the significance of his work was its demonstration of the fact that "blood reaches even the densest parts of bones."

Sir Hans Sloane (1660–1753), being a member of the Royal society, may well have heard Belchier read his papers but whether he did or not, human vanity being what it is, we may assume that he read the volume in which they were published because he had a paper of his own in that same volume. In any event, it is certain that he was aware of the work because he brought it to the attention of his friend, Duhamel (1700–1782), a French gentleman-naturalist who was a member of the French Academy of Science. In 1739, three years after Belchier's second paper, Duhamel published a paper entitled, "Concerning a Root which Dyes the Bones Red," in which he described the experimental feeding of madder to chickens, turkeys, pigeons and pigs, and other publications followed over a period of four years. Sir Arthur Keith (1866–1944) in his 1919 book, "Menders of the Maimed," summarizes Duhamel's work as follows:[23] "Duhamel [though] not trained in Medicine discovered that there was a problem of bone growth and showed the world how such a problem should be solved. He turned the chance observation of an English surgeon into a powerful instrument of research. He showed that bone is stained with madder only as it is being laid down. He showed that a bone grew in thickness by circumferential deposition of plate upon plate; that a long bone grew in length at its extremities; that the deepest layer of the periosteum was the maternal tissue of bone."

John Hunter (1728–1793) was an eight-year-old boy on his father's farm near Glasgow [12,13,29] when John Belchier first ate pork from madder-fed pigs and he did not come to London to begin studying anatomy with his elder brother, William (1718–1783), until five years after Duhamel's later publications. Twenty years more elapsed before he himself fed madder to animals, as Belchier and Duhamel had done more than a quarter of a century earlier. In October, 1798, five years after Hunter's death, his brother-in-law, Sir Everard Home (1756–1832), reported briefly to the Society for the Improvement of Medical and Chirurgical Knowledge on the results of Hunter's madder-feeding experiments and said that Hunter had been lecturing on the subject since approximately 1765.[19] It was not until 1841, however, that the posthumous publication of his papers provided in Hunter's own words the following conclusions based on those experiments:[28] "Young bone may always be said to grow, even the part that seems to be already formed; for at first it is growing longer, thicker and denser; so that there is always new matter added until it is at its full growth. But in the full-grown state, it would appear from the circumstance of reddening a whole bone by feeding the animal with madder, that a bone, although completely formed, yet is changing its earth, and probably every other part. This effect, however, is much slower than in the growing bone. This would show that the madder does not act as a dye upon the earth which is already deposited in the bone, but only upon that matter that is every day deposited; and as there is a great deal more deposited in a young bone than in an old one in a given time, in the same proportion must it dye sooner than an old one. The new matter that is deposited in an old bone is to make up for the waste that is daily going on in it; but in a very old bone the waste is more than the repair."

It has long been known that crude shellac contains a reddish pigment which, on precipitation with metallic salts, produces an insoluble dye originally called a "lac," a term long since corrupted to "lake." Several other dyestuffs, such as cochineal and madder, form similar lakes, the particular color depending on the particular metallic salt or mordant that is employed. Dyes that form lakes on reaction with mordants are known as mordant dyes and have long been employed for imparting permanent colors to fabrics, particularly cottons.

In the experiments of Belchier, Duhamel and Hunter, madder that had been laked with calcium was found only in bone that

had been laid down during the period of feeding, and yet alizarin, which is the active principle of madder, is in common use today as a tissue stain for bone of all stages of development.[10] Why is it that, in tissue sections, alizarin lakes with calcium wherever it may be, whereas in vital staining with madder the lake appears only in growing bone? Almost surely the answer is this: As madder is absorbed from the alimentary tract into the blood stream, it lakes promptly with calcium circulating in the blood, leaving no free or unbound madder. Those parts of the skeleton that are laid down in laked calcium are red and those parts laid down before madder feeding begins or after it has been discontinued are white. There is no "bleeding" of the color from the red zones to the white zones because the calcium lake is highly insoluble.

Von Recklinghausen (1833–1910) introduced silver impregnation of fixed tissue cells in approximately 1863[25] and later von Kóssa[11] employed silver nitrate impregnation to bring out deposits of calcium phosphate in tissue sections. Modified by Mallory, Lillie, and McLean and Bloom, the method is in active use today. Like alizarin staining, silver nitrate impregnation is not truly specific for calcium salt, but it does indicate the presence of deposits of inorganic material by turning them black, and under all ordinary conditions calcium phosphate is the only inorganic material found in bones.[26]

Silver impregation can be employed to enhance the radiopacity of the bones of small laboratory animals and used in this way has proved helpful in working out the ossification patterns in fetal pigs.[18] Fresh fetuses fixed forty-eight hours in 95 per cent alcohol and then soaked from forty-eight to seventy-two hours in a 0.5 per cent aqueous solution of silver nitrate show little deposition of silver in the soft tissues but a very dense deposit in all calcified portions of the skeleton.

Since the work of Wegner[39] in 1872, it has been known that the feeding of approximately 0.15 milligrams of yellow phosphorus a day will cause changes in the bones, if the experimental animals are young and growing, but none if they are adult. These changes, which were demonstrated by direct inspection of the bones taken from his experimental animals and from a few children dying of rickets after trials of phosphorus therapy, consisted of the laying down of an abnormal amount of bone at the growing ends of the shaft and in the case of chickens throughout the medullary cavity. In 1918 Phemister[31] reported the roentgen evidence of phosphorus feeding, and since then the dense zones at the ends of shafts and about epiphyses have become familiar sights to all of us. They constitute a sort of vital staining of growing bone and, like tree rings, enable us to make at least rough judgments as to the rate of growth.

With the improvement of microscopes and the perfection of tissue stains, much new information has been gathered concerning the morphology and function of the cells that make up periosteum, perichondrium, bone, cartilage and marrow, but many of the concepts that were widely accepted at first have not stood the test of time. Experiments based on tissue transplants meant little until the role of infection was understood and controlled, and growth experiments were apt to be complicated by inadequate feeding of laboratory animals in the days before the discovery of the vitamins. The present-day vogue for tagging elements that are to be metabolized by growing bone is beginning to clarify the picture of bone growth, but of this and many other important pieces of modern work there is time to say almost nothing. Following up Phemister's observation that bone sometimes develops in kidney stones which are attached to the renal pelvis and other reports of ectopic bone in sclerotic arteries, the dura mater, calcified tuberculous lesions in the lung, the tonsils, etc., C. B. Huggins conducted a series of experiments. In the dog there was production of bone, complete with

haversian systems and red marrow, when epithelium from the bladder or other parts of the urinary tract was transplanted into fascia or fascia was transplanted into the epithelium of isolated bladder pouches or the two types of tissue were transplated together into the spleen.[20] On the other hand, no bone production occurred in or about transplants of sterile bone from which all organic elements had been removed.[21] Why urinary tract epithelium should be able to stimulate certain fibroblasts to differentiate into osteoblasts and why acute experiments with calcium deposits fail to produce bone whereas long-standing deposits apparently may produce it are questions that remain to be answered.

One idea has worn well for the century and a half since John Hunter's time—namely, the concept that even after bone has reached full growth it continues to be an actively living tissue, one that is constantly being torn down and constantly rebuilt.[22] One of the most dramatic proofs of this fact lies in the remarkable changes that occur in the marrow cavities of the shafts of the long bones of ovulating pigeons.[6] In the male and the resting female, the marrow cavity is devoid of bone, but with the development of an ovarian follicle cancellous bone proliferates from the inner surface of the cortex until, just before ovulation, it fills the cavity completely. As the egg leaves the ovary and enters the shell gland, a rapid and extensive destruction of marrow cavity bone occurs clearly for the purpose of mobilizing calcium needed for the production of the shell. This special case of bone destruction and reconstruction following one another in rapid cycles provides an excellent opportunity for studying the reversible metamorphosis of fibroblasts into osteoblasts and osteoclasts, and, if it were needed, supplies additional proof that bone is a specialized form of connective tissue.

Recent remarks by Franklin McLean[38] concerning the present state of our knowledge of the physiology of bone may be summarized as follows: The amount and physical state of the calcium in the circulating blood are important factors in the calcification of bone, but we know little as to why, with all the tissues of the body subjected to the same circulation, only those specifically designed to become bone undergo calcification. It is currently popular to assume that enzymes are concerned in the process, but Robison's concept of a rather simple mechanism involving alkaline phosphatase has been abandoned even by him. There is experimental proof that certain tissues will undergo in vitro calcification even after treatment that must have destroyed all enzymes, but perhaps enzymes prepare tissue to receive calcium from the blood and, having done so, are no longer needed.

In the embryonic period, during growth, and in maturity specialized fibrous tissue elements lay down noncalcified precursory tissue which becomes bone by the act of undergoing calcification. Normally these two processes, the laying down of the calcifiable tissue and the calcification of it, are practically simultaneous but if for any reason there is a generalized or local dearth of available circulating calcium, some of the precursor matrix remains uncalcified for a while, constituting the so-called osteoid tissue.

DISEASED BONE

Skeletal disease becomes roentgenologically detectable only when it has caused considerable disturbance in the normal processes of growth and repair. Acute pyogenic osteomyelitis usually requires a week or more to become discernible and the subperiosteal hemorrhages of scurvy commonly remain invisible until therapy is started.[16] It goes without saying that we detect disease by observing alterations from normal, but it is less well appreciated that, conversely, the findings in disease may be employed to test and extend our knowledge of the normal. For the light that may be thrown on skeletal physiology, let us consider certain aspects of pyogenic osteomyelitis, tertiary syphilis and osteosarcoma.

Staphylococcus osteomyelitis of a long

bone, which before the advent of the antibiotic drugs was one of the commonest skeletal lesions, dramatizes the bone-building power of the periosteum. The in-infection produces vascular congestion, edema and an inflammatory exudate which spreads through the bone, killing the osteocytes and marrow cells, sometimes only in parts of the bone, sometimes in all of it. Spread is easiest along the medullary canal, but usually the cortex is involved as well with perforation in one or more places, following which pus collects beneath the periosteum, stripping it away from the shaft. With the subsidence of the acute phase, the pyogenic granulation tissue attacks and absorbs dead spongiosa and separates as sequestra those parts of the cortex that have died, and the periosteum lays down a new cortex, the so-called involucrum. Usually the repair processes, though active, are not completely successful and with repeated cycles of pus formation and stripping of periosteum there is built up a thick, irregular, multilayered involucrum, penetrated here and there by cloacae. Surgical removal of one side of such an involucrum and the removal of the necrotic bone frequently serves to turn the tide and leads to a final subsidence of the infection, following which the remainder of the involucrum gradually is reworked into a shaft looking surprisingly like the old one that has been destroyed.

Tertiary syphilis or gumma of bone sometimes is accompanied by subperiosteal proliferation, but in particular it illustrates the activity of the cells that usually are concerned with the reworking of normal spongiosa and cortex. Roentgenologically we see multiple small areas of bone destruction in close proximity to bone production, seldom with large sequestra. Histopathologically, the small areas of bone destruction correspond to small masses of gummatous tissue which have become necrotic through involvement of their blood vessels, and surrounding these areas new bone is being laid down. Since the lesion is relatively painless, there is little or no osteoporosis of disuse and so the normal bone retains its normal density.

In osteosarcoma we frequently see the periosteum elevated by tumor tissue and thus stimulated to a resumption of its bone-building function, as in osteomyelitis, and also we see the production of reactive bone by stimulated spongiosa, as in the case of gumma; but in addition to this, as Brunschwig and Harmon[8] have pointed out, the bone-producing metastases of this tumor supply proof that the osteoblast is an active bone-building agent and not a mere passive bystander. It must be admitted that it is not common for the metastases of osteosarcoma to produce bone but they sometimes do, and twenty years ago these authors were able to collect records of 39 such cases in man and 1 case in a laboratory animal. It is believed that at least part of the bone at the primary site and in skeletal metastases of osteosarcoma is tumor bone rather than reactive bone, this belief resting on reasonably secure ground, but belief gives way to established fact when bone develops in the metastases to such tissues as the skin or the liver. Just as carcinoma of the bile ducts tends to produce atypical bile ducts in its metastases and numerous other tumors tend to reproduce in their metastases the tissues from which they spring, so do the malignant osteoblasts of osteosarcoma on metastasizing produce tumor bone just as their nonmalignant precursors produce normal bone.

In diseases such as rickets, scurvy, osteomyelitis and tuberculosis, we know the cause and cure, and in sketetal neoplasm at least have gained a fairly good understanding of the mechanism of spread. There are other skeletal diseases, however, in which our ignorance of essentials remains profound and of these there is no better example than the condition to which we currently apply the term "fibrous dysplasia of bone." About the best that can be said for this term is that most physicians know what it means and it assists in avoiding the confusion of this condition with the skeletal manifestations of hyperparathyroidism. The existence of such confusion is not surprising because both conditions were

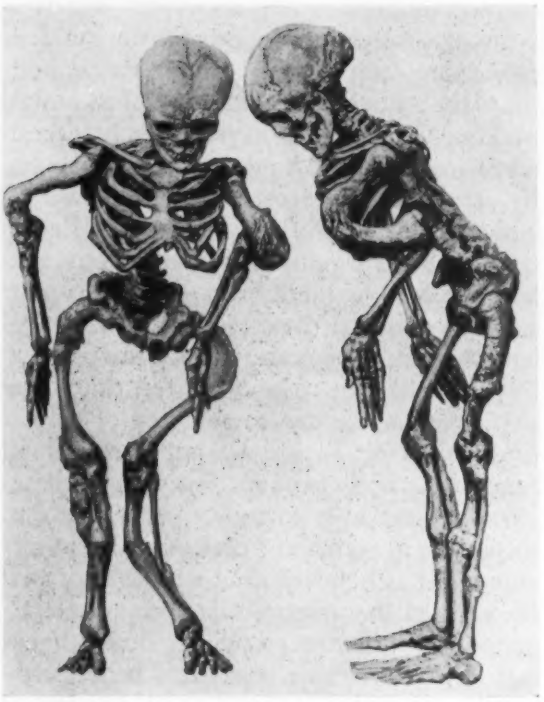

FIG. 2. Fibrous Dysplasia of Bone. Von Recklinghausen's Case 6, reproduced by Armed Forces Institute of Pathology from von Recklinghausen's Monograph published in 1891. Employing superb and painstaking technique, the Institute's photographers have prepared an illustration vastly better than the original from which it was taken.

represented in von Recklinghausen's 1891 monograph,[35] and for a time several different skeletal diseases, including hyperparathyroidism and fibrous dysplasia, were lumped together under the term "von Recklinghausen's disease of bone." The lesions of fibrous dysplasia are most characteristic when they involve tubular bones. One end of a long bone may be involved while the rest remains normal, or the entire shaft may be diseased. Those regions that are involved may show merely alteration of the trabecular pattern in some portions, with complete loss of the pattern in other portions. Usually the cortex of involved regions is thin and, particularly in the femur, weakness of the shaft is apt to result in characteristic lateral bowing (Fig. 2). The vault and base of the calvarium, the jaws, pelvis, ribs and spine sometimes are involved and when lesions in the base of the skull are progressive there may be severe damage to the brain and optic nerve. When an involved long bone is laid open, one finds the medullary canal grossly dilated and filled with firm, dirty gray, fibrous tissue which, on being rubbed between the fingers, has a gritty feel, and under the microscope there is seen a stroma of white, fibrous, connective tissue in which there are irregular branching strands of embryonic bone. Surgery is the only known means for treating fibrous dysplasia and even it is employed principally for the management of fractures and the correction of deformities. In a few instances, complete extirpation of the abnormal fibrous tissue has seemed to expedite arrest of the disease and sometimes the disease is self-limited. More often, and particularly in severe cases, there is slow but progressive deterioration, though, unlike Paget's disease, the complication of malignant degeneration has not been observed. It is easier to say what fibrous dysplasia is not than to say what it is. It appears to be not an endocrine disturbance, not a bacterial infection, and not a neoplasm, and the most common guess is that it belongs in the category of congenital diseases. On the other hand, though histopathologically the lesions do not appear to be neoplastic and there is no evidence that they metastasize, still their local response is something like neoplasm and their tendency to spread and involve neighboring bone can sometimes be arrested by surgery.

DEAD BONE

In an age when almost none of us brings to the study of medicine a sound training in the classics, medical terms drawn from Latin or Greek can be troublesome, and the word "necrotic" is such a troublesome term, particularly when it is applied to bone. Necrotic bone is dead bone—just that and nothing more—but, unfortunately, in the absence of specific education to the contrary, many physicans on hearing the term "necrotic" think of softening, purulence

and disintegration, whereas when sizable segments of bone are killed en masse the most striking feature is the ability of such pieces to retain their normal hardness for long periods of time, yielding only very slowly to disintegration and absorption.

The endless metamorphosis which, since Hunter's time, has been recognized as characteristic of living bone stops abruptly with the loss of blood supply, and the metamorphosis that occurs much later, when blood vessels from neighboring living tissue work their way into the interstices of dead bone, produces an entirely different roentgenological appearance. Living bone maintains its density in health, becomes osteoporotic with disuse or sclerotic with overuse, but these changes fail to occur in bone that is dead and their absence is about all we have on which to base a roentgenological diagnosis of bone necrosis.

It is no easy matter to determine just how long mature bone will survive the loss of its blood supply but certainly the period must be very brief. Explants of fetal bone do survive and grow in suitable culture media and the evidence is good that some of the cells of the marrow, endosteum and periosteum of autoplastic grafts of mature bone do remain alive by virtue of surrounding tissue juices during the period that they are acquiring a new blood supply. Interpretation of transplant experiments is complicated, however, by the possibility that whether they contain living elements or not, pieces of grafted bone may "induce" the formation of new bone in the bed in which they are placed in something like the manner that the optic cup of the marine newt *Triton* on transplantation will induce the skin to produce a lens in regions far removed from the normal location of the eye.[37] Autoplastic grafts are employed primarily to provide mechanical strength plus an optimum framework in which the osteogenic tissues of the host can lay down new bone. If, in addition to these functions, such grafts bring to the new site surviving osteogenetic elements that start at once on the process of substitution, so much the better.[14] It is established that fresh, unwashed grafts are better than those that have been subjected to salt solution, to say nothing of less physiological media, and that autoplastic grafts are superior to those that are isoplastic or heteroplastic. These facts do not prove, however, that any considerable portion of a graft that "takes well" remains alive and, on the contrary, there is roentgenological and operative proof that exactly the reverse is true. The surgical and reontgenological means of demonstrating that a given piece of bone is dead have been set forth in a classical publication by Phemister;[32] the roentgenological evidence is partly direct, partly indirect. The indirect evidence is the failure of dead bone to share in disuse osteoporosis that may involve the neighboring bone, and the direct evidence is the characteristic pattern of "creeping substitution" in dead bone that has been invaded by blood vessels from neighoring living tissue. The inindirect sign fails if there is not enough pain or imposed restriction on activity to produce regional osteoporosis or if death occurs after osteoporosis has developed, and the direct sign may be overlooked if for any reason it is impossible to obtain roentgenograms of adequate quality. This term, "creeping substitution," appears again and again in Phemister's writings from as early as 1915[30] to as late as 1951.[34] In his 1915 paper, "Necrotic Bone and the Subsequent Changes Which it Undergoes," he says, "Necrosis due to circulatory disturbances is best exemplified by bone transplants . . . only the unossified portions, that is, the periosteum and medullary contents, and the more superficially located osseous cells survive. The great bulk of the compact bone undergoes necrosis. The surviving osteogenetic cells proliferate, revascularization of the haversian canals occurs, the old cortex is gradually absorbed and replaced by new bone. This is the so-called creeping substitution which was first pointed out by Barth."

I have examined a considerable number of Barth's excellent and clearly written

FIG. 3. Nonunion of Fracture of Neck of Femur. Even though the head survives, a fracture of the neck of the femur may fail to unite. (*A*) Appearance of fresh fracture. (*B*) Four months later; no necrosis of head but union has not occurred. (*C*) Twenty months after injury and sixteen months after living bone graft; union has now occurred.

Patient M. D. (No. 40976), female, aged forty-five.

publications on bone transplants[2,3] but nowhere can I find the adjective "creeping" used in connection with "substitution" or "transformation" though the concept certainly is there. In 1893 Barth[2] says in regard to the replacement of a bone transplant, "We have to do here not with a resorption in the usual sense and a subsequent substitution by new construction; on the contrary, we are concerned here, if you will, with a sort of metaplasia with a substitution of the dead by living bone tissue." Barth believed that the substitution depended almost exclusively on ingrowth from surrounding living bone, and Phemister credits Axhausen with being the first to demonstrate that the periosteum and endosteum of the transplant survive and are the principal agents in generating the new bone which replaces the dead bone. By 1937 Axhausen and Bergmann in their section of Henke and Lubarsch[1] were using the term *schleichender Ersatz* but they give Phemister as one of their references so it is possible that he coined the term in English and they translated it into German. Phemister made no such claim and I am arguing simply from negative evidence. Regardless of the authorship of the term, the credit for the concept should go, as Phemister has indicated, to Barth and to Axhausen.

Uninfected autoplastic bone grafts are a special case in which a minimum of time elapses betweeen surgical interruption of the blood supply and the transference of the graft to a bed where it is bathed in blood identical to that previously received through its own blood vessels, and even under these conditions the main portion of the graft dies. In most of the situations in which we have to deal with sizable pieces of dead bone, there is no tissue juice to nourish periosteal and endothelial cells and so they too die, leaving the ingrowing tissues from neighboring live bone as the sole base from which creeping substitution occurs. When dead bone is not in contact with living tissue capable of providing it with a new blood supply, it retains its density indefinitely and this situation sometimes obtains in the case of large sequestra in pyogenic osteomyelitis or in part or all of the head of the femur in tuberculosis of the hip joint. Dead human fetuses, whether retained in the uterus or extruded into the peritoneal cavity, suffer no decalcification of their skeletons, and Lawlah and Hodges[24] have shown that in rabbits the bones of a fetus once calcified

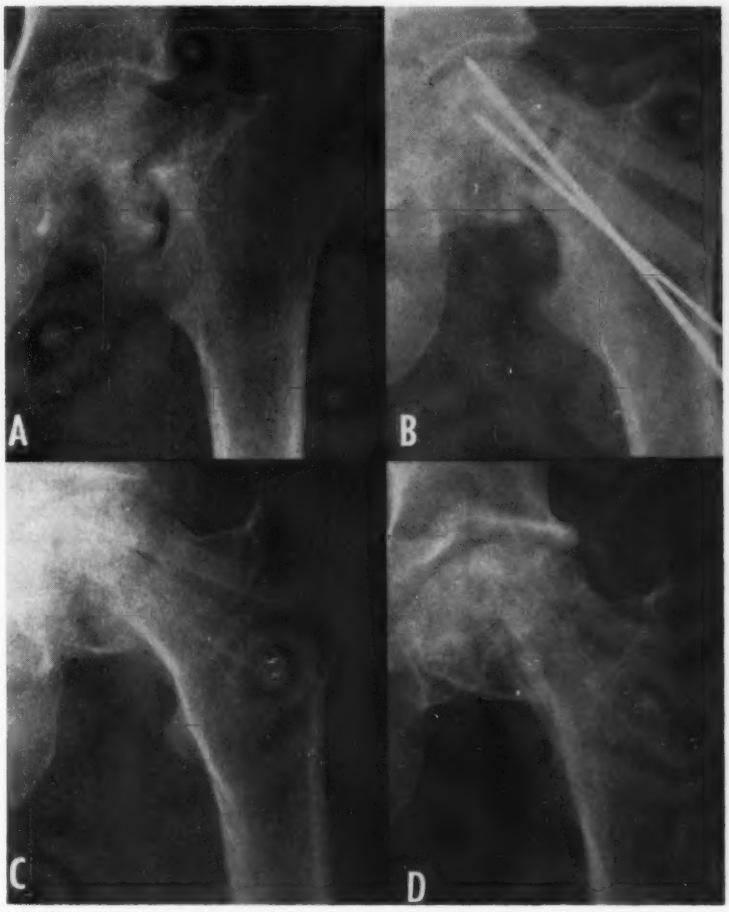

Fig. 4. Nonunion of Fracture of Neck of Femur. When the head dies, nonunion is more common. (*A*) Nine months following fracture, the dead head is being replaced very slowly by creeping substitution; union has not occurred. (*B*) Wire pins have been inserted for mechanical strength and living bone grafts to expedite replacement of head. (*C*) Eight and one-half months following operation, replacement is progressing satisfactorily. (*D*) Seven years following operation, a good clinical result has been obtained.

Patient H. A. (No. 193163), female, aged fifty-two.

do not lose their calcium, even though the fetus die and be retained in the body for more than a year.

There are three conditions in which the roentgenological diagnosis of the occurrence and the fate of necrotic bone is of particular clinical importance and in which, conversely, the careful study of the course of events has added to our knowledge of bone physiology. I refer to the repair of fractures of the neck of the adult femur,[33,36] aseptic necrosis of the head of the femur in growing children, and subchondral necrosis of the fractured carpal scaphoid.

The head of the femur receives most of its blood from the branches of the anterior and posterior circumflex arteries traveling in the capsule of the neck and a much smaller amount from arteries of the round ligament. When the neck is fractured near the head, all of these vessels are in jeopardy. Sometimes enough of them escape injury so that circulation in the proximal fragment is maintained, but in most cases the bone and the articular cartilage of the head suffer aseptic necrosis. Even when the head survives there may be nonunion (Fig. 3), but more commonly union occurs by virtue of callus growing from both fragments to bridge the fracture line. When all or most of the proximal fragment dies, union is less common because callus grows only from the living distal fragment. When the head dies and union does occur, either spontaneously or following surgical procedures, the dead head is gradually infiltrated by new blood vessels which break down and remove old dead bone and replace it by new (Fig. 4, 5, and 6). This is a most desirable phenomenon but while it

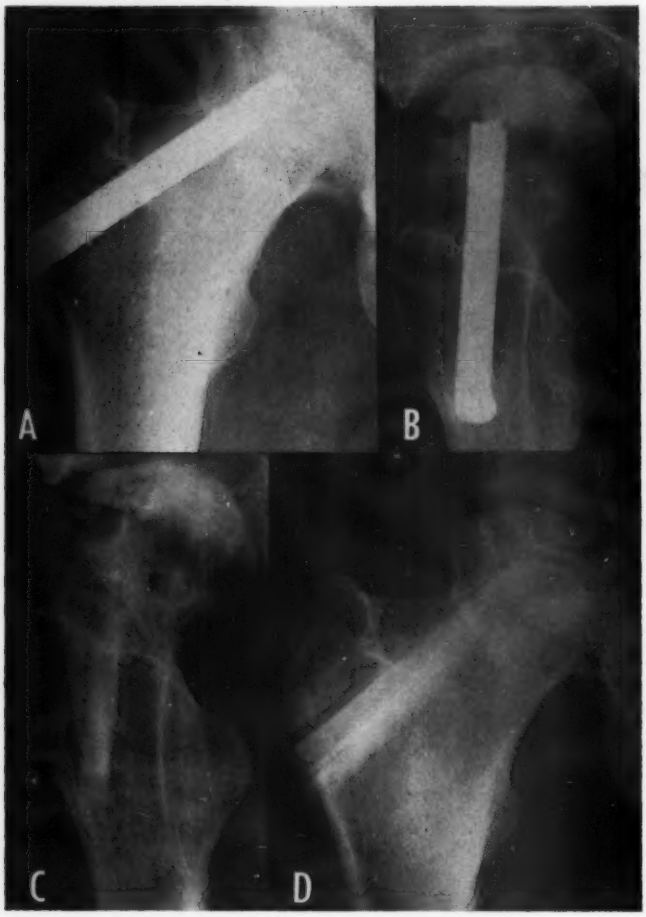

FIG. 5. Interruption of Blood Supply to Head of Femur. Aseptic necrosis develops promptly but may go unrecognized for a long time. (*A*) and (*B*) Frontal and lateral views. Appearance of right hip three years after nailing a fracture of the femoral neck; a large segment of the femoral head has died and failed to be replaced. (*C*) and (*D*) Lateral and frontal views taken a few days after the removal of the nail and the insertion of live bone grafts.

Patient R. Y. (No. 419626), male, aged thirty-one.

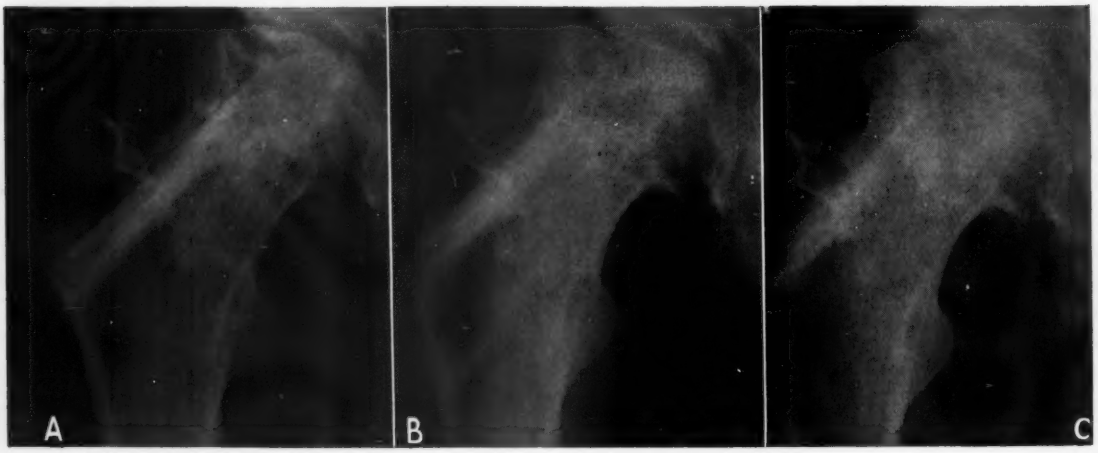

FIG. 6. Same case as Figure 5. (*A*) Ten months later. Most of the head is undergoing replacement but a small button of cortex is separated from the rest of the head. (*B*) Three and one-half years after operation. Reconstruction more nearly complete. (*C*) Four and one-half years after operation. A satisfactory clinical result has been obtained.

Fig. 7. Interruption of Blood Supply to Head of Femur. Late collapse of necrotic femoral head. (*A*) Fresh fracture of neck of right femur. (*B*) and (*C*) Frontal and lateral views, following the insertion of threaded pins.

Patient F. S. (No. 325222), female, aged sixty-six.

is going on the head is mechanically weaker than it was when it was made up wholly of dead bone, and if it is subjected to weight-bearing it is apt to suffer pathological fractures ranging all the way from slight flattening of the articular cortex at the weight-bearing point to complete refracture through the neck. Sometimes such secondary fractures coming on months or even years after the initial injury constitute the first intimation that the head is necrotic and many physicians have been misled into assuming that the head has survived for a long time after the vascular injury and has died only later at about the time of the observed collapse (Fig. 7, 8, and 9).

Fresh fractures of the femoral neck are usually pinned with threaded wires. If union does not occur, autoplastic grafts are introduced regardless of whether the head is alive or dead. When the head is alive, these grafts provide a bridge for callus which, for some reason, has not developed before, and when it is dead they serve in addition as canals which expedite the growth of the tissue elements that replace the dead head by the mechanism of creeping substitution. In these latter cases union usually becomes solid in three months, but it may be necessary to protect the head against weight-bearing for two or three years if a well-functioning hip is to be accomplished. Sometimes the damage to the blood supply of the femoral head and neck is caused by dislocation rather than fracture and sometimes by irradiation,[7] but regardless of the cause of the vascular disturbance the repair processes are identical in type and vary only in degree and rate.

In young children, the loss of the blood supply to the femoral head causes necrosis only of the bone whereas the articular cartilage usually survives by virtue of nourishment derived from synovial fluid. If weight-bearing is avoided while the dead bone is being transformed into new, little permanent deformity results.

In fractures of the scaphoid of the wrist, both fragments may survive and unite like any other fracture, but sometimes one or both fragments become devascularized. Theoretically, when one scaphoid fragment survives it might be expected to be able to serve as a base for the replacement of the dead half through creeping substitution, but frequently the process is so slow that surgical removal of the dead portion becomes the procedure of choice.

CONCLUSION

In September, 1899, the editor of *The Western Clinical Recorder*,[17] in the course of a criticism of therapeutic nihilism, said,

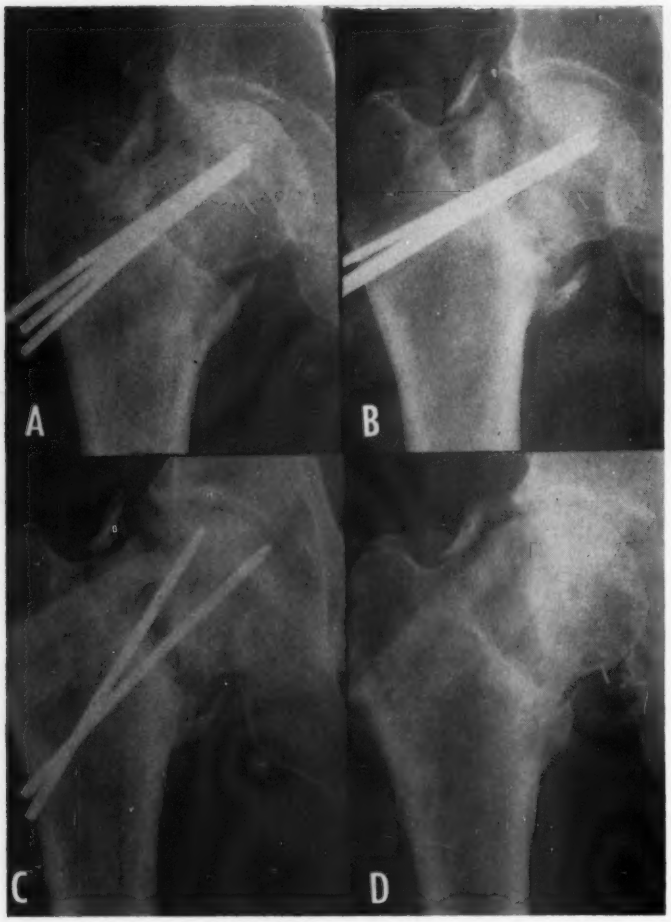

FIG. 8. Same case as Figure 7. (*A*) Eight months. (*B*) Eleven months after injury. Union has not occurred. The head has become necrotic. (*C*) New wire pins have been inserted for strength, together with two living bone grafts to stimulate union and replacement. Of the latter, the upper one unfortunately has not penetrated deeply into the head. (*D*) Nine months after the grafting. The lower two-thirds of the head is undergoing replacement but the upper third is not, presumably because the graft did not reach into it.

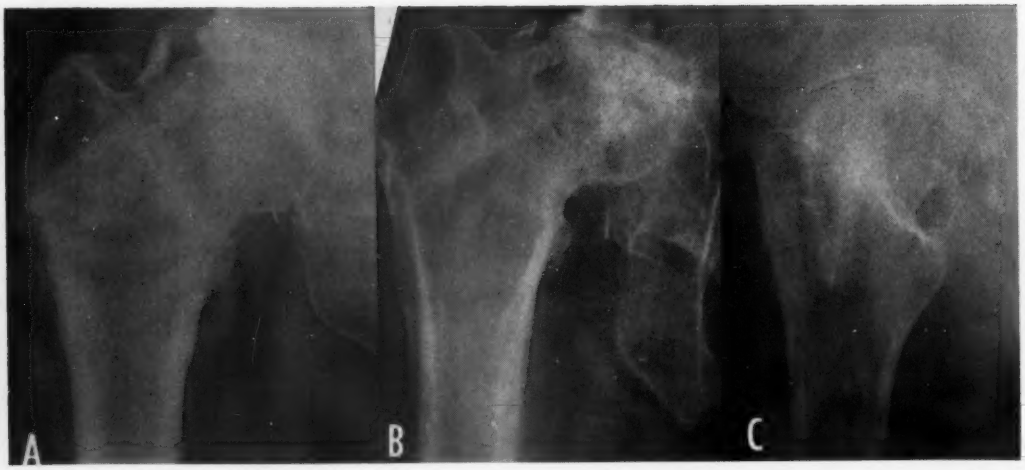

FIG. 9. Same case as Figure 7. (*A*) Two and one-fourth years after operation. The result seems to be good. (*B*) and (*C*) However, five years after operation there is collapse of the upper third of the head in the region that had not been reached by one of the living bone grafts. It is a common error to misinterpret such findings as indicative of aseptic necrosis coming on late after the injury.

"The human body is in many of its most important particulars an unknown field to the wisest men of the day. We have as yet not even begun to speculate concerning many of the manifestations of the vital processes actuating the body. . . . The animal body never can present the simple conditions of a chemical reaction of a demonstration in physics. The existing forces are so manifold and complex that we are only just beginning to find out not simply how little we know but [how] much we do not know about them."

In the year 1894, roentgenology was nonexistent and beyond comprehension; and at the time that this editorial was being written roentgen rays were still merely a medical curiosity. In the half century that has followed, roentgenology has become enormously useful, not only for examining the bones of the intact living organism but also in the study of laboratory specimens; and surgery, pathology, physiology and roentgenology working together have provided us with a far better understanding than our fathers had of the way in which bones grow, sicken and die. The fact remains, however, that in this year of 1953 we would do well to remember the editorial of 1899 and recognize that we are only just beginning to find out how much we do not know about the formation, growth, disease and death of bone.

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Vol. 71, No. 6

PUNCTATE EPIPHYSEAL DYSPLASIA (CHONDRODYSTROPHIA CALCIFICANS CONGENITA)*

REPORT OF CASE WITH NINE YEAR PERIOD OF OBSERVATION

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PUNCTATE epiphyseal dysplasia is a rare disorder of bone growth apparently belonging to the general group of chondrodysplasias. The first case with roentgen studies was reported in 1914 by Conradi.[2] Fairbank reported 2 cases in 1927[3] and subsequently in 1949[4] reviewed the findings in 16 cases which he accepted as satisfactory examples of the disease. He called the condition dysplasia epiphysialis punctata. A variety of other terms have been employed including chondrodystrophia calcificans congenita and chondroangiopathia calcarea seu punctata. The latter was suggested by Cocchi[1] as being descriptive not only of the roentgenographic appearances but of the histopathologic as well. This term is favored by Haynes and Wangner[5] who reported a recent case. The simpler designations, punctate epiphyseal dysplasia or dysplasia epiphysialis punctata seem adequate for clinical purposes.

The disorder is characterized roentgenologically by the appearance of multiple small calcific areas within the hyaline cartilages giving them a stippled appearance. These areas of calcification apparently develop during intrauterine life, being present at birth, and are usually discovered during early infancy. Haynes and Wangner reported an instance where antepartum examination of the mother showed a bony maldevelopment of the fetus and a suggestion of stippling of the epiphyses. Later she delivered of a typical cyclops monster but no postpartum roentgenography could be obtained. Twenty-one months later a second pregnancy was investigated roentgenologically with similar findings. Postpartum examination revealed a typical achondroplastic dwarf. In addition, there were spotty calcific deposits throughout the epiphyseal cartilages. The infant died three hours after birth. Early death is frequent in this disorder and of the 16 cases reviewed by Fairbank half are known to have died, all but one before reaching the age of twelve months. Thus opportunities for observing the progress of the condition have been limited. Raap[7] in 1943 was able to follow several siblings for a period of nearly four years and noted that the abnormal calcifications disappeared at about the age of three years. A similar observation was made by Jorup.[6] It is of interest to note that Raap's patients were apparently normal in all other respects, while in many of the cases reported other developmental variants or acquired disease have been present.

The clinical signs have been variable. According to Fairbank, dwarfing of the short limb type is usually but not invariably present. The affected epiphyses tend to be enlarged. Flexion of some joints with limitation of motion has been noted in some. In the British cases bilateral congenital cataract has been a frequent finding. Mental retardation, general weakness and failure to thrive are common. A distinct familial tendency has been noted.[5,7,8]

On roentgenographic examination the epiphyses show the presence of multiple discrete calcified areas giving a peculiar stippled appearance as if ossification were occurring from multiple centers. The areas vary in size but usually are minute. The epiphyses most frequently affected have been those of the upper and lower ends of the femur, the upper end of the tibia and the upper end of the humerus. However,

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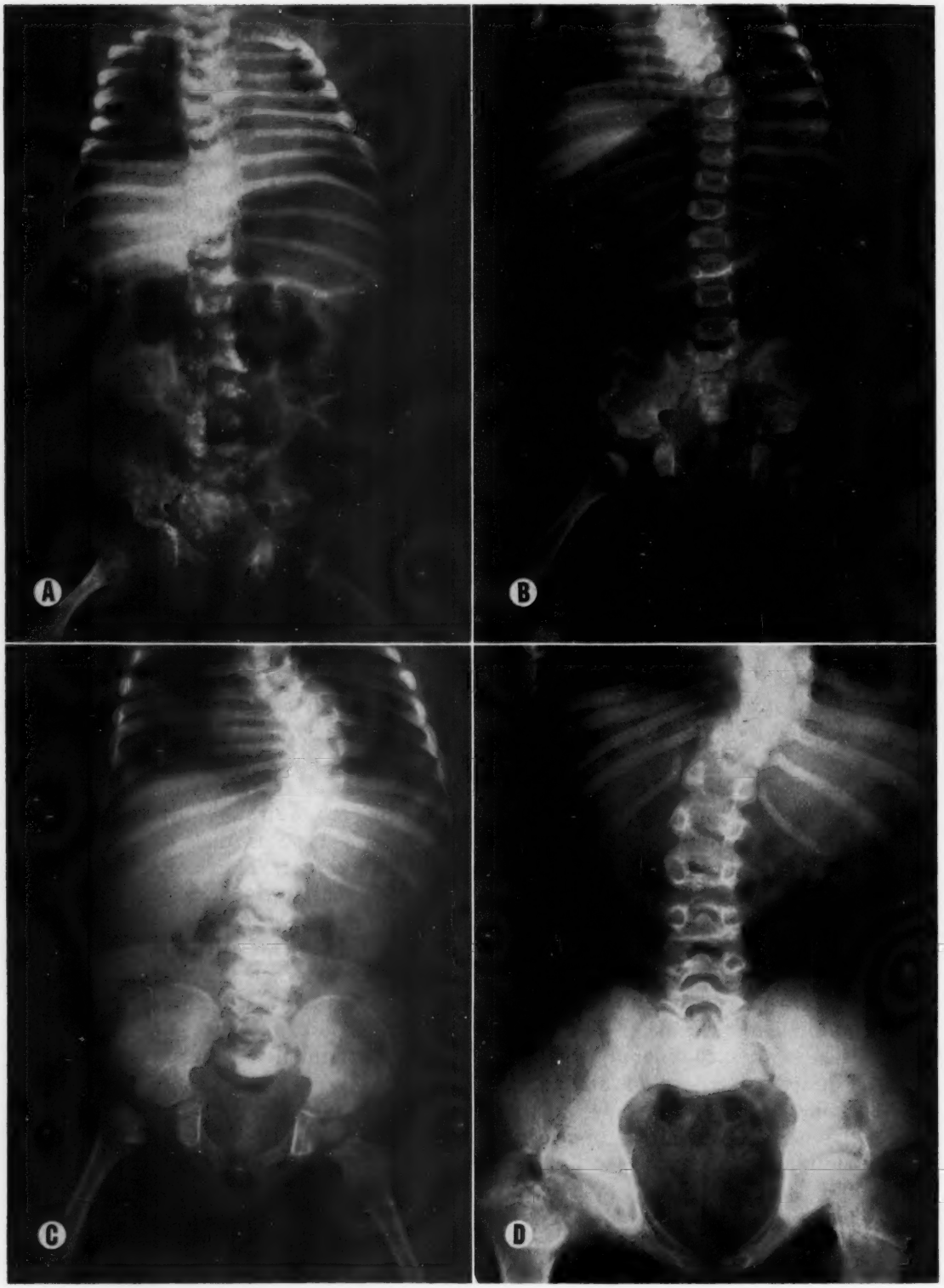

FIG. 1. (*A*) Appearance of the spine at the age of one month. Widespread stippled calcification in all cartilaginous areas. (*B*) At the age of eight months most of the spots have disappeared. Several of the mid-dorsal vertebrae have abnormal contours. (*C*) A year later only a few hazy areas of calcification remain in the right acetabulum. The dorsal scoliosis is more pronounced and the epiphysis for the head of the right femur has not begun to ossify. (*D*) At the age of nine years and three months there is persisting dorsal scoliosis. The right femoral epiphysis has ossified but the hip is dysplastic. All other bones are relatively normal.

Fig. 2. (*A*) The right lower extremity at the age of one month showing extensive areas of abnormal calcification in the hip, knee and foot. (*B*) Seven months later the calcific foci have decreased in number and size. Normal ossification centers have appeared in all areas except the hip. (*C*) A year later (age 20 months) a few hazy areas of calcification remain. The capital femoral epiphysis is unossified.

the stippling may be extremely widespread involving practically all cartilaginous areas. Deposits have been noted in the thyroid cartilage and in the hyoid.

We have had the opportunity of observing a case of punctate epiphyseal dysplasia with extensive involvement of the skeleton from the age of one month to nine years and three months. Because of the few serial studies which have been reported in the literature and the information it yields concerning the progress of the disorder, we are reporting the case at this time.

CASE REPORT

R. G., female infant, born February 18, 1939, was one month old at the time of the first admission to the hospital on March 23, 1939. The baby was born prematurely and weighed 5 11/16 pounds at birth. Delivery was difficult. There were three other children in the family who were apparently normal at birth. One died at the age of two years from pneumonia. The other two were alive and well. The patient was admitted because of a shortening of the right leg noted at birth. Physical examination revealed a shortening of the right lower extremity. There was a pilonidal cyst. The neck was

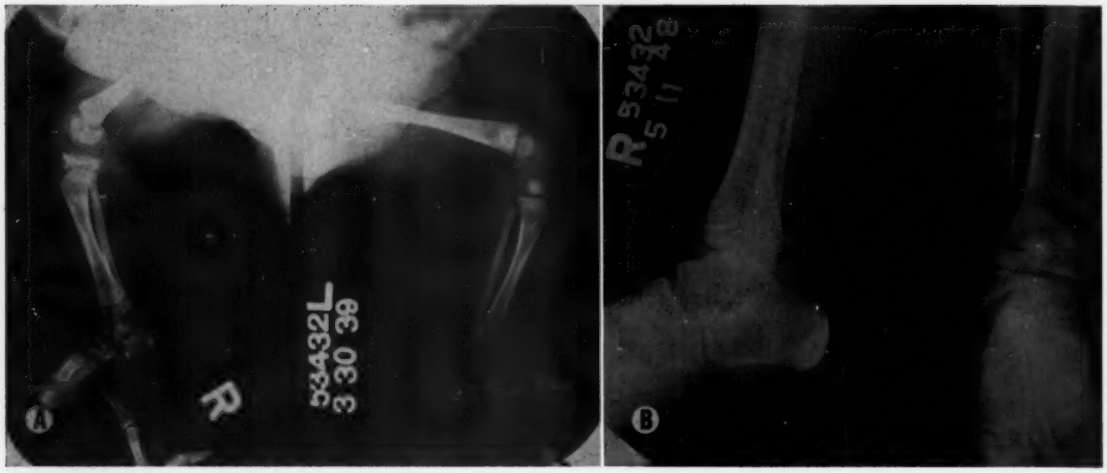

FIG. 3. (*A*) Lateral view of the legs at the age of one month. The abnormal foci are more numerous in the shortened right lower extremity. (*B*) Right ankle at the age of nine years and three months. The bones have ossified normally.

short. No other pertinent findings were recorded. The results of routine laboratory studies were within normal limits. The blood serology was negative. The blood serum calcium was 10.4, phosphorus 6.0 and alkaline phosphatase 3.3. The basal metabolic rate on two occasions was plus 7 and plus 8. Roentgenograms of the skeleton are reproduced in Figures 1 to 4. These demonstrated the presence of innumerable tiny calcified spots scattered widely throughout the cartilaginous portions of the skeleton. The deposits were most numerous in the epiphyses of the right lower extremity and there was a distinct shortening of this extremity as compared to the left. No treatment was given or recommended.

The second admission occurred on October 26, 1939. Repeat roentgen studies showed a distinct regression in the number of calcified densities and those remaining seemed definitely smaller. A scoliotic deformity of the dorsal spine was becoming apparent and malformation of several of the mid-dorsal vertebral bodies was noted. Subsequent roentgen studies were made on November 7, 1940, and on May 11, 1948. In 1940, when the child was twenty-one months old, all of the abnormal calcific foci had disappeared except those in the right lower extremity. Here a few remained and there was an absence of the normal femoral capital epiphysis. The right lower extremity remained shortened and the dorsal scoliosis had increased. In 1948 roentgenograms of the spine showed the persisting scoliosis due to the malformed dorsal vertebrae. All stippling had disappeared in the right lower extremity, and in the ankle and foot the bones seemed to be entirely normal in contour. In the right hip the capital epiphysis had ossified but was somewhat misshapen, the femoral neck was short and there was a varus deformity. The acetabulum was shallow.

Since October, 1939, the clinical examinations have been done in the Out-Patient Department or in one of the traveling orthopedic clinics. The child's development has been normal except for the scoliosis and the short leg deformity.

COMMENT

Roentgen observations of this child cover a period of her life from the age of one month to nine years and three months. She had a short leg type of dwarfism limited to one lower extremity. This extremity remains short but subsequent growth has been nearly equal to the opposite one. There was a rapid disappearance of the abnormal calcific foci so that within seven months after the initial observation many of them had disappeared. Those that remained were smaller. At the same time normal centers of ossification made their appearance and, with a few exceptions, developed normally. Eventually all of the calcified foci disappeared. It appears, therefore, that the abnormal areas of

Fig. 4. (*A*) Right upper extremity at the age of one month. Calcific foci are noted particularly at the upper end of the humerus and in the carpal region. (*B*) At the age of eight months the foci are less numerous. Normal carpal centers are developing. (*C*) At the age of twenty months there has been further decrease in the number of abnormal foci.

calcification are formed during intrauterine life, that they tend to disappear rapidly, that they do not represent normal foci of ossification occurring in multiple form, and that subsequent ossification of the cartilage usually occurs in a normal manner. Excluding the dwarfed right lower extremity, ossification centers for the epiphyses developed normally. As can be noted in the knees, the epiphyseal centers for the femur and tibia formed and developed in the presence of the calcified foci. Exceptions to normal osseous development are to be noted in the right hip and in the dorsal spine. Growth of several of the dorsal bodies was asymmetrical and ossification of the right capital femoral epiphysis was delayed. This growth disturbance seems to be due to an associated defect in ossification and not to the presence of the stippling *per se*. The stippling in the rest of the spine was quite similar to that noted in the dorsal region and yet all other vertebrae developed normally. This was true in other areas as well. Some authors have considered the disorder to be an abortive type of achondro-

plasia. In our case the chondrodysplastic tendency seems to have been limited to a few of the dorsal vertebrae and the right lower extremity.

SUMMARY AND CONCLUSIONS

Punctate epiphyseal dysplasia (chondrodystrophia calcificans congenita) is a rare disorder characterized by the occurrence of numerous small foci of calcification in many of the cartilaginous portions of the infantile skeleton. These form during intrauterine life, subsequently decrease in size and disappear. If there is no associated disorder of enchondral bone formation (chondrodysplasia) normal epiphyseal centers form and develop, and growth proceeds without interruption leaving no skeletal defects. Dwarfism of the short leg type often is present. In our case this was limited to one lower extremity together with abnormality of growth of several of the dorsal vertebrae. While the stippling and the abnormality of growth seem to be related, the stippling of itself does not appear to be the sole cause of the dwarfing. There is no evidence in our case that punctate epiphyseal dysplasia is a precursor of osteopoikilosis either of the spotted or striped variety or that it is related in any way to the fragmented epiphyses of cretinism. In the case reported roentgen observations of the skeleton were carried out over a period of approximately nine years.

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ROENTGENOGRAPHIC EXAMINATION IN MENINGIOMA OF THE TUBERCULUM SELLAE OR OLFACTORY GROOVE

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CHANGES in the bone that result from intracranial meningioma should be of great interest to the physician. An adjacent meningioma can produce eight varieties of pathologic changes in the skull, according to Cushing and Eisenhardt.[8] The first variety is that of increased vascularity, the second is that of bony erosion, and the remaining six varieties are those of different manifestations of bony proliferation. The most common and characteristic variety encountered by them consisted of a slight bony thickening on the inner table of the skull.

Detection of these bony changes in roentgenograms of the skull is of utmost importance because they indicate the exact position of the associated meningioma. The fact that meningiomas of the vault may produce huge exostoses makes it evident why the earliest pathologic study of the bony changes produced by meningiomas was that of Louis in 1774. In 1864, Cleland reported a case in which a meningioma arising from the region of the olfactory groove was encountered at necropsy, and mentioned the presence of an exostosis of the base of the skull. Cushing observed in 1922 that hyperostoses, while most commonly involving the vault and the greater wing of the sphenoid, may occur on the cranial base. The report of Heuer and Dandy concerning roentgenographic localization of brain tumor stressed the changes which occur in the vault, but failed to mention changes of the base. While Cushing observed that hyperostoses may occur at the base of the skull, he failed to cite an example.

Camp[3] in 1924 reported the case of a meningioma that had arisen just posterior to the olfactory groove and had produced a large osteoma which was visible in the roentgenogram. Sosman and Putnam in 1925 reviewed the roentgenographic changes in 95 cases of intracranial meningioma. In addition to the already mentioned pathologic changes of increased vascularity, erosion, and proliferation, they mentioned calcification within the tumor. They found what they considered recognizable changes in the roentgenograms of 47 of their 95 cases. Calcification occurred in 3 cases. They stated that the tumors about the sella are apt to cause nonspecific distortion and destruction of the clinoid processes. Four of the 12 suprasellar tumors showed these changes, and 3 of the 7 tumors arising in the region of the olfactory groove showed changes from normal.

In 1931 Camp[4] summarized the roentgenographic findings associated with meningiomas arising from the region of the olfactory groove and the tuberculum sellae. These findings are: (1) formation of an osteoma at the point of origin of the tumor, (2) localized erosion of the cribriform plate of the ethmoid bone, the wings of the sphenoid bone, the sulcus chiasmatis, and the tuberculum sellae, (3) erosion of the

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posterior clinoid processes, (4) enlargement and erosion of the sella turcica and (5) calcification within the tumor.

The significance of posterior displacement of a calcified pineal gland was emphasized by Olivecrona and Urban when they reported that it occurred in 4 of of 9 patients with meningioma of the olfactory groove. The essential features of the roentgenographic changes as we now know them were thus established. While there have been several subsequent accounts of the roentgenographic changes observed in a series of meningiomas arising from the olfactory groove, little has been written about the changes produced by meningiomas of the tuberculum sellae. Emphasis has been placed upon the pneumoencephalographic and ventriculographic changes occurring in these lesions by Adson, Dyke and Davidoff, Hamby and Gardner, and others. Thus in 1934, Bucy and Kredel reported the occurrence of hyperostosis in association with a meningioma of the tuberculum sellae as quite unusual. This is perhaps largely accounted for by the fact that Cushing and Eisenhardt,[7] in earlier writings concerning the "chiasmal syndrome," emphasized that in the presence of a meningioma arising from the tuberculum sellae, the sella appears normal in the roentgenograms.

In the bone adjacent to a meningioma of the tuberculum sellae the surgeon and the pathologist frequently have found changes which were not recognized in the roentgenogram. We must consider that approximately 20 per cent of all intracranial meningiomas arise in the region anterior to the sella, posterior to the foramen cecum and near the midline (an area of about 4 by 2 cm.). The roentgenographic detection of abnormalities in this small region requires an intimate knowledge of normal anatomy and variations. Since the structures are in or near the midline, the opportunity to compare the normal with the abnormal side is usually not present.

As in all roentgenographic interpretation, it is essential that the roentgenograms be of good technical quality. The presence of a chiasmal or anterior basilar tumor is usually suspected clinically, and attention is thus focused upon this region. When such is the case, it is a grave mistake to rule out the presence of a tumor on the evidence presented by roentgenograms of poor quality or roentgenograms made with the subject poorly positioned. The routine roentgenogram of the skull will normally show the necessary details. Stereoscopic lateral view roentgenograms should be taken with one view a direct lateral and the other a view with the tube shifted in the coronal plane. In addition to the conventional posteroanterior and anteroposterior (Towne) projections, the posteroanterior view at an angle of 107 degrees, originated by Granger, is valuable for demonstrating the anterior portion of the roof of the sphenoidal sinus. Laminagraphy also has proved valuable for the disclosure of changes in the structure of the sphenoid and ethmoid bones.

In the lateral view careful attention should be paid to the midline structures. Note is made of the shape and density of the tuberculum sellae; also, attention is paid to the sulcus chiasmatis, the limbus sphenoidalis, the planum sphenoidale and the ethmoid spine of the sphenoid bone, all of which are found anterior to the tuberculum and in the order listed, beginning posteriorly. It is important that these structures are seen normally in a line of definite sharpness. This line, anterior to the ethmoid spine, follows two courses. One is seen inferiorly as the cribriform plate and the other is seen superiorly as that portion of the orbital plate over the ethmoid air cells. These two lines again unite at the posterior portion of the frontal sinus to form the inner table of the frontal bone. While thin and often broken, the general contour of these lines can be seen. The shadow of the crista galli may not always be seen in the lateral view.

In the conventional posteroanterior views one can normally see the cribriform plate (which lies between the olfactory

bulbs and the air passages of the nose), the crista galli, the jugum sphenoidale with the underlying sphenoid sinus, the orbital portion of the frontal bone overlying the ethmoid cells, and the anterior clinoid processes. The posteroanterior view at an angle of 107 degrees demonstrates the so-called G line. Special views of the optic foramen are frequently necessary for completion of the roentgenologic examination.

CHANGES OBSERVED IN THE PRESENT SERIES OF CASES

The roentgenograms of 51 patients who had meningiomas arising in the region of the tuberculum sellae were examined. Twenty-eight of the patients were found to have hyperostoses in the region of the tuberculum sellae (Fig. 1). These hyperostoses were recognized on the basis of change in the bone of the tuberculum sellae, or often on the basis of change in the sulcus chiasmatis or the limbus sphenoidalis. The bone was thickened, but often it had a spongy appearance rather than an increased density. Eight of the meningiomas presented roentgenographic evidence of calcification; this calcium was scattered throughout the tumor rather than in the capsule (Fig. 2). Four tumors produced local erosion which was visualized in both lateral and Granger views. Sellar erosion as occurs with extrasellar pressure was present in 9 cases. The roentgenographic appearance was within normal limits in 9 cases.

Fig. 1. Typical small dense osteoma arising from the tuberculum sellae and associated with a meningioma. The meningioma was removed and the osteoma was rongeured away. The patient was alive and well twenty years after operation.

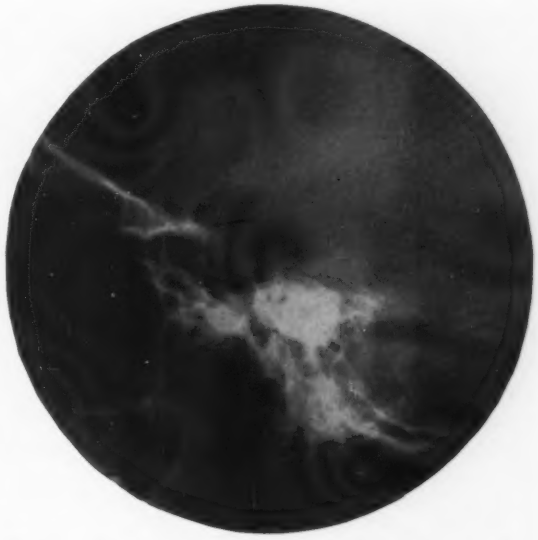

Fig. 2. Small osteoma of the tuberculum sellae. Visible flecks of calcium are scattered throughout the meningioma.

Roentgenograms of the skulls of 42 patients who had meningiomas arising in the region of the olfactory groove were examined. In 16 there was evidence of hyperostosis. As previously noted by Erikson, such hyperostosis occurs in the large majority of cases, on the superior surface of the posterior portion of the ethmoid bone, at the spheno-ethmoid junction. Six of the meningiomas were calcified and all of these were associated with hyperostosis (Fig. 3*a* and *b*). In 3 of the cases there was local erosion. Erosion or depression of the cribriform plate must be interpreted with great care because of the normal variation of this structure. The presence of erosion of the anterior portion of the planum sphenoidale is a much more reliable sign. Erosion of the sella as evidence of extrasellar pressure was present in 16 cases.

Thirteen cases of meningioma of the ol-

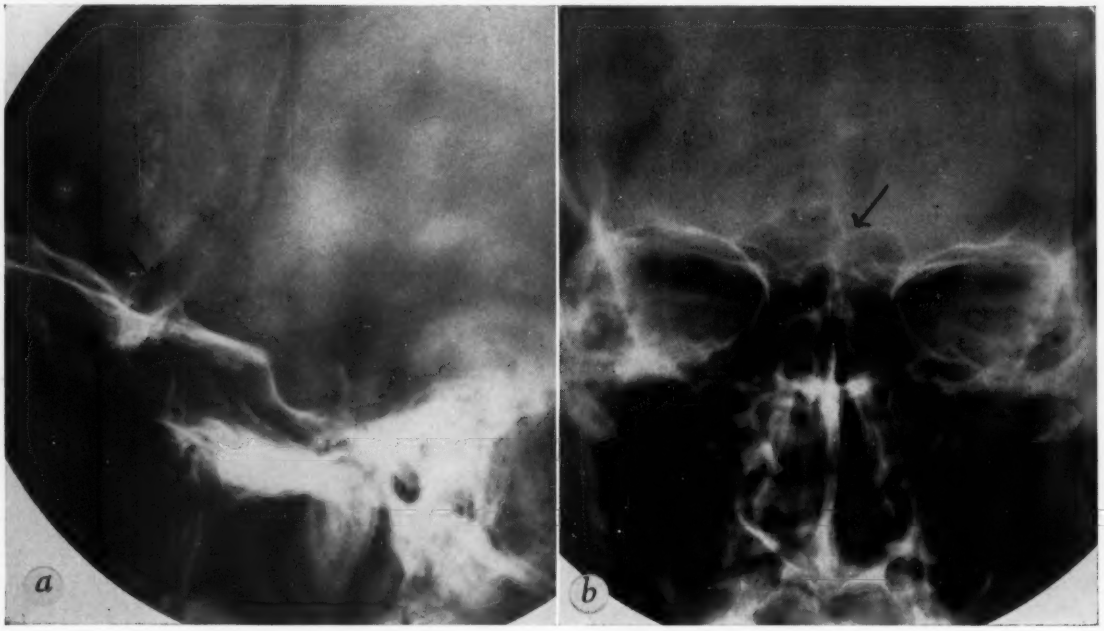

FIG. 3*a* and *b*. Lateral and anteroposterior views of a "spongy" osteoma arising from the region of the ethmoid spine. Calcification is evident throughout the large, overlying meningioma of the olfactory groove.

factory groove were selected as suitable for measurement of pineal displacement. With the methods of Vastine and Kinney, the pineal body in 2 cases was found to be displaced posteriorly. True posterior displacement of the pineal body depends, of course, on the mass of the lesion and surrounding edema. Detection of this displacement has been discussed by Fray, Dyke and Lilja subsequent to the time of Vastine and Kinney's report. One of these methods should always be used to measure a calcified pineal body in a case of suspected basofrontal tumor.

SUMMARY

Roentgenographic changes which may be seen in association with meningiomas arising in the region of the olfactory groove and tuberculum sellae are discussed, and data on series of tumors occurring at these two sites are presented. In each group of tumors the localizing characteristic of calcification of the tumor, hyperostosis or erosion was encountered. One or more of these localizing roentgenographic changes were observed in 33 of 51 cases of tuberculum sellae tumor, and in 25 of 42 cases of olfactory groove tumor. While it is true that pneumoencephalography, angiography and even exploratory craniotomy may have to be done in order to establish the correct diagnosis, a careful study of well-made roentgenograms of the skull often suggests the correct diagnosis.

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SOME FACTORS WHICH AFFECT THE VALUE OF CAROTID ANGIOGRAPHY IN THE DIAGNOSIS OF BRAIN TUMOR*

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INTRODUCTION

CEREBRAL angiography, as performed by the percutaneous injection of water soluble excretory contrast media into the carotid artery, is one of the most valuable additions to neuroroentgenologic methods of diagnosis. Its advantages include technical expedience, the absence of disturbance of cerebrospinal fluid dynamics and, at times, the opportunity to diagnose the pathologic nature of the lesion even preoperatively. Granting these advantages of cerebral angiography for the patient and surgeon alike, nevertheless a critical knowledge of the limitations of the procedure is necessary. It is the purpose of this paper to review some of the anatomic, roentgenologic and clinical factors which restrict the value of cerebral angiography in the diagnosis of brain tumor and to suggest criteria for the selection of patients suitable for angiographic examination.

MATERIAL

This study is based upon the review of the case histories of 100 consecutive patients with verified brain tumor and the objective interpretation of their angiograms. In all of the patients with negative angiograms and in some patients with positive angiograms other neuroroentgenologic procedures were performed, usually cerebral pneumography. During the same period, carotid angiograms were performed upon 40 additional patients suspected of having brain tumor. In the latter group each angiogram was negative and no substantiating evidence of the presence or absence of cerebral tumor is available. These cases are excluded from the study.

All but one of the patients had lesions situated above the tentorium and in either cerebral hemisphere or near the midline at the optic chiasm. One had a posterior fossa tumor, an acoustic neurinoma, which clinically masqueraded as a supratentorial lesion as a result of obstructive hydrocephalus. In 81 instances angiography disclosed the lesion (Table I). In 19 patients angiography failed to reveal the lesion.

Fifty-five of the 100 patients with brain tumor had neoplasms of the suprasellar region or frontal area and in these cases evidence of the lesion was found in the angiogram without exception (Fig. 1). It is noteworthy that 2 patients had a clinical diagnosis of tuberculum sellae meningioma but suprasellar aneurysms were disclosed and, because of this, possible surgical catastrophes were averted. In the majority of patients with temporal lobe tumors angiographic diagnosis was likewise successful.

TABLE I

THE SUCCESS OF CAROTID ANGIOGRAPHY IN THE DIAGNOSIS OF 100 CONSECUTIVE VERIFIED TUMORS IN VARIOUS PORTIONS OF THE BRAIN

Locus of Tumor	Angiogram Positive	Angiogram Negative
Suprasellar	21	0
Frontal	34	0
Temporal	23	2
Parietal	2	8
Occipital	0	4
Paraventricular		
Thalamic	0	4
Corpus callosum	1	0
Posterior fossa	0	1
TOTAL	81	19

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Two patients, in whom angiography failed to disclose a lesion, had temporal lobe tumors that were posterior in position and deformed only minor branches of the middle cerebral artery. These changes in the angiogram are not considered to be of diagnostic value in the case of either patient, even in retrospect.

Carotid angiography was almost as impressively without diagnostic dependability in the demonstration of tumors in all other portions of the cerebrum as it was successful in the disclosure of suprasellar, frontal and temporal tumors. In 12 of 14 patients with parietal and occipital neoplasms the angiogram was essentially negative, and in 4 patients with deep-seated tumors near the midline, which involved the thalami and basal ganglia, nothing indicative of tumor was found, save evidence suggesting hydrocephalus in 2 instances. Thus, the number of diagnostic failures of carotid angiography in the presence of cerebral tumor amounted to approximately 20 per cent of the total. This percentage of failures is a reflection of the inherent limitations of the procedure and not an indictment of technique as performed in experienced hands, or the quality of clinical interpretation. The experiences related by Egas Moniz,[4] Lima,[6] Ecker,[3] Torkildsen,[10] Engeset,[5] Curtis,[1] and List, Burge and Hodges[7,8,9] are well known and, in general, their criteria of localization of brain tumor, modified by some original concepts, were applied in the series of cases herein reported. Some of the minor changes in form described in the literature as characteristic of posterior tumors, however, are considered too tenuous to justify such a formidable procedure as intracranial exploration.

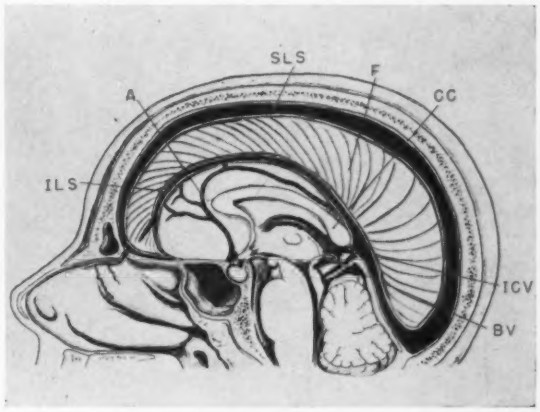

Fig. 2. The Head in Median Section. (A) Anterior cerebral artery; (F) falx cerebri; (BV) basal vein; (CC) corpus callosum; (ICV) internal cerebral vein; (ILS) inferior longitudinal sinus; (SLS) superior longitudinal sinus. The position of the anterior cerebral artery inferior to the level of the free edge of the falx allows herniation of the vessel into the contralateral half of the cranial cavity as a result of tumor in any portion of the cerebrum. Lateral displacement often is the only abnormality of the anterior cerebral artery produced by a tumor and is not always of value in the localization of the lesion.

Fig. 1. Olfactory Groove Meningioma. The cerebral portion of the internal carotid artery is displaced backward and compressed. The anterior cerebral artery is elevated and the convexity of the proximal part is reversed. The superior, posterior and inferior limits of a subfrontal tumor are well defined in the angiogram.

ANATOMIC DISCUSSION

The study of cerebral angiology teaches, and the present review of carotid angiograms performed for the diagnosis of brain tumor merely confirms, that accurate angiographic diagnosis results only for tumors in certain anatomic locations. Since angiographic localization of brain tumor is dependent upon displacement of normal vessels, or the visualization of abnormal vascular branches in a tumor area, evidence of a new growth most often is shown when

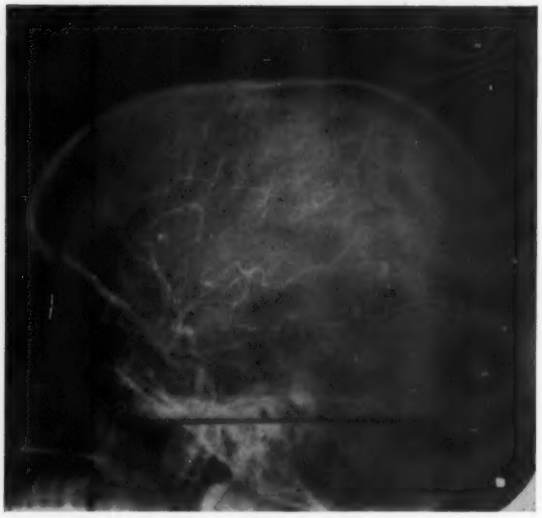

FIG. 3. Parietal Meningioma (same case as Fig. 4) The lateral left carotid angiogram fails to disclose evidence of a tumor despite satisfactory opacification of the small branches. In frontal projection only displacement of the anterior cerebral artery far to the right of its normal position was demonstrated. The examination provided insufficient information for intracranial exploration, since lateral displacement alone of even the rostral portion of the anterior cerebral artery is not considered diagnostic of a frontal mass.

the neoplasm is situated along the course of the major carotid branches. Diagnostic failure results when tumors lie outside of the distribution of the larger carotid arterial branches.

Of considerable anatomic significance in defining the limitations of carotid angiography is the relation of the anterior cerebral artery to the falx cerebri (Fig. 2). Throughout the greater part of the length of the anterior cerebral artery and of its main terminal continuation, the pericallosal artery, the vessels are below the level of the free edge of the falx and near the midline. Not only frontal tumors will produce displacement of the anterior cerebral artery across the midline. Tumors originating in any part of one hemisphere, which create diffuse edema of that hemisphere, likewise will cause displacement of the anterior cerebral artery beneath the falx to the opposite side of the cranial cavity. This edema results frequently when tumors compress the major posteriorly draining veins of the cerebrum, and such tumors ordinarily are situated far from the frontal area. Once the anterior cerebral artery has become incarcerated beneath the falx it can no longer be elevated or otherwise deformed locally in the region of the tumor (Fig. 3 and 4). Lateral displacement of the anterior cerebral artery, therefore, is not always of value in the localization of brain tumor. At the point where the displaced anterior cerebral artery passes under the edge of the falx it is often compressed, with the result that the parieto-occipital course is not well seen. With incarceration of the anterior cerebral artery the diagnosis may depend, by exclusion, upon the form of the middle cerebral artery alone. Many branches of the middle cerebral artery are in close relation to the inner table of the skull, and as a result, displacement by tumor cannot occur in all directions. In addition, the exact inclination of the sylvian fissure and of the middle cerebral vessels varies somewhat with the shape of the head.

CLINICAL DISCUSSION

Carotid angiography appears to be most valuable for the confirmation of a clinical diagnosis of cerebral tumor. Carotid angiography is not always the procedure of choice to demonstrate a clinically unlocalized tumor, nor is it useful always as a screening procedure for the detection of a suspected tumor in the patient upon whom an adequate neurologic examination cannot be carried out. The proper selection of patients for carotid angiography depends primarily upon neurologic examination and secondly upon findings in plain roentgenograms of the head.

It is not the purpose of this paper to discuss the localization of brain tumor by neurologic examination even though brief reference to certain localizing symptoms and signs is necessary. Patients who present themselves primarily because of sensory epileptic seizures, scintillating scotomas or other irritative disturbances of the parietal and occipital cortex are considered poor candidates for satisfactory carotid angi-

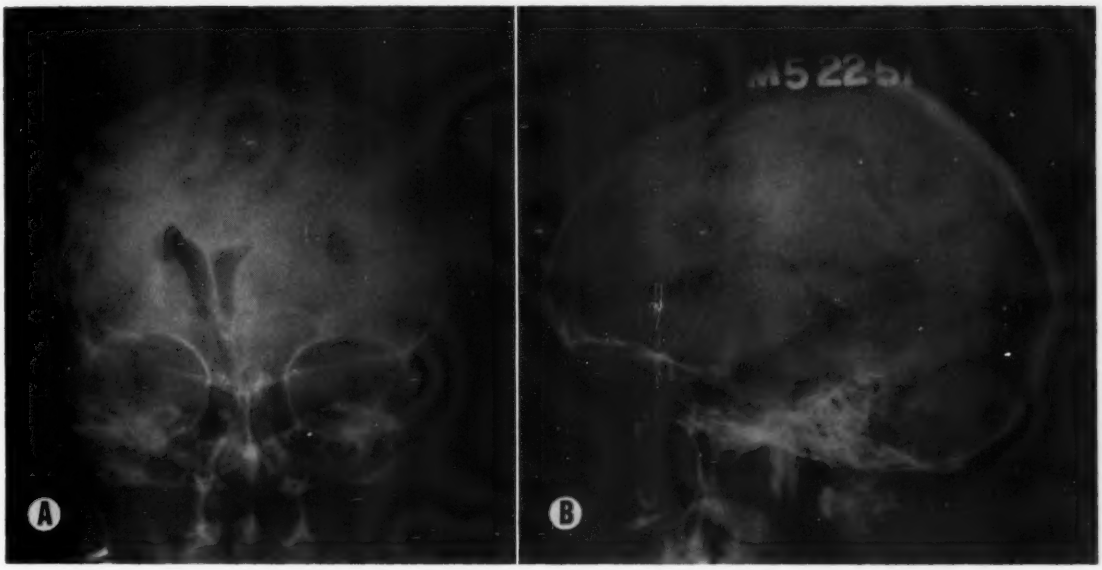

Fig. 4. Parietal Meningioma (same case as Fig. 3). The lateral ventriculogram (*B*) discloses deformity of the posterior portion of the body and atrium of the left lateral ventricle which is the result of an expanding lesion of the parietal area. The frontal film (*A*), made with the patient supine, reveals displacement of the foremost portion of the left lateral ventricle beneath the falx, even though the neoplasm is in the posterior part of the cranial cavity.

ography. Involuntary movements and muscular rigidity often indicate a lesion near the midline in the region of the thalami and basal ganglia, which are not embraced by major carotid branches (Fig. 5).

It may be worth emphasizing how often one particular phase of the neurologic examination, namely plotting of the visual

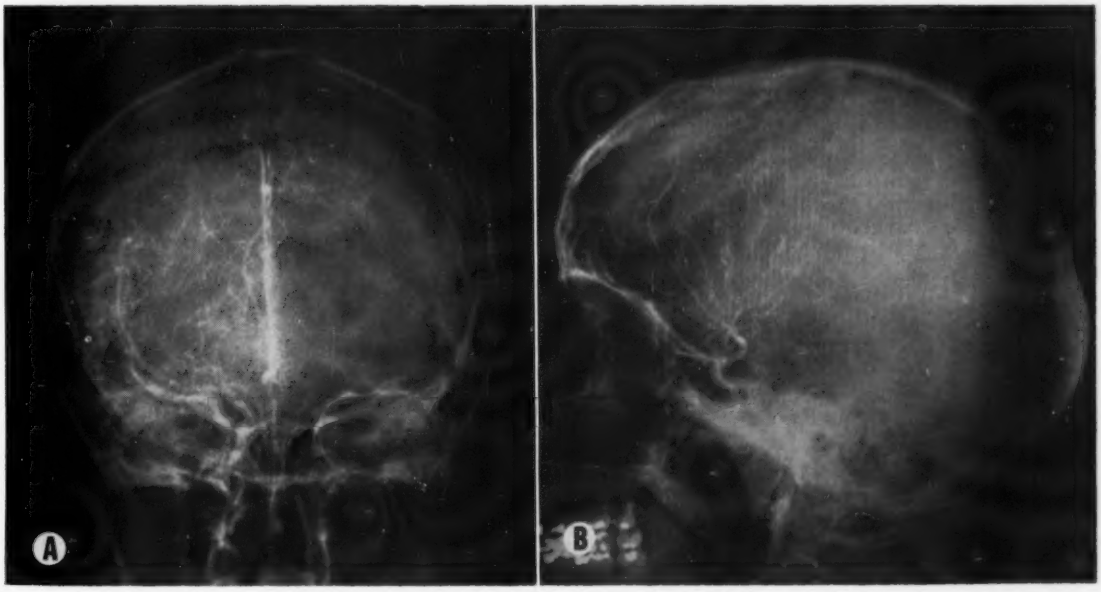

Fig. 5. (*A*) and (*B*) Thalamic Astrocytoma. The arc of the anterior cerebral artery is widened, which suggests hydrocephalus, but nothing to indicate the exact location of the underlying pathologic process is revealed by angiography. Ventriculography disclosed an expanding lesion of the thalamus and basal ganglia, which elevated and deformed the floor of the right lateral ventricle. Dilatation of the lateral ventricles resulted from compression and occlusion of the third ventricle.

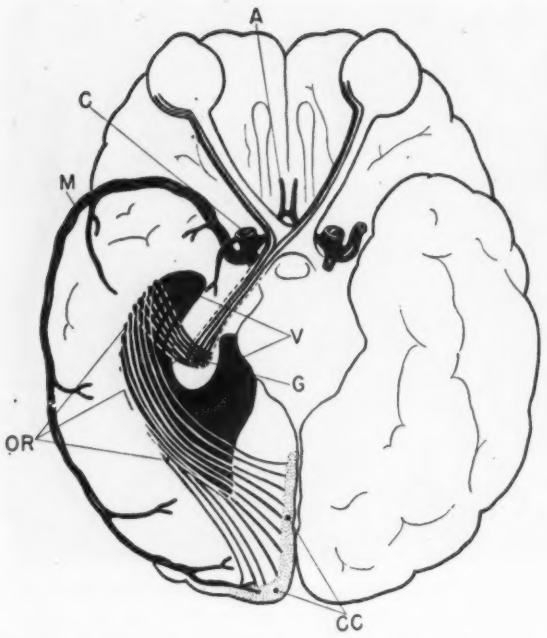

FIG. 6. Disposition of Optic Pathway, Internal Carotid Artery and Lateral Ventricle. (A) Anterior cerebral artery; (C) internal carotid artery; (G) geniculate body; (M) middle cerebral artery; (V) lateral ventricle; (CC) cingulate cortex; (OR) optic radiations. Tumors which involve the optic chiasm and produce bitemporal hemianopia usually deform the anterior portion of the circle of Willis, which can be demonstrated readily by carotid angiography. Tumors which involve the optic radiations and produce homonymous hemianopia deform more consistently the ventricular system than the middle cerebral artery.

fields, contributes to accurate tumor localization and the proper selection of patients for carotid angiography (Fig. 6). Patients with suprasellar tumors, who exhibit bitemporal hemianopia, are ideally suited for the demonstration of the pathologic process by angiography (Fig. 7). A homonymous hemianopia, on the contrary, is not always of localizing value, especially if it is complete. It is not uncommon for patients with small tumors of the temporal lobe or large tumors of the occipitotemporal area to have negative carotid angiograms. While homonymous hemianopia may suggest the possibility of an expanding lesion in the temporal lobe which can be demonstrated by angiography, the intimate relation of the optic radiations to the lateral ventricles suggests that pneumography may be the procedure of choice when such a visual disturbance is present (Fig. 6).

Some concern is felt regarding the fate of the 40 patients suspected of having brain tumor who had negative angiograms and, as a result, were discharged with undiagnosed neurologic disease. Occasional members of this group presented themselves because of seizures and visual disturbances of such nature that a tumor was suspected at the time of admission to the hospital. The material aforementioned suggests that carotid angiography alone is inadequate to exclude the presence of cryptic cerebral neoplasm.

In plain head roentgenograms enlargement of the sella turcica, hyperostosis of the skull or pathologic intracranial calcification near the course of the branches of the internal carotid artery are findings which favor the use of angiography as a definitive neuroroentgenologic diagnostic procedure. Downward, backward or marked lateral shift of the pineal suggests the possibility of a gross frontal or temporal tumor (Dyke[2]). Such displacements are promising for the success of angiography. Foward displacement of the pineal gland and displacement of the choroid plexus most often are the result of a tumor situated posteriorly and these findings are considered contraindications for the use of carotid angiography to investigate their cause.

SUMMARY

1. Carotid angiograms, when interpreted in a completely objective manner, have resulted in correct diagnosis in 81 of a group of 100 consecutive patients with verified brain tumor. The negative examinations do not indict technique or interpretation but are the result of anatomic limitations of the procedure.

2. Success of the carotid angiogram is enhanced by careful selection of patients for angiographic investigation. Patients with neurological findings which point to posterior or deep tumors are not best suited for evaluation by angiography.

3. Plotting of the visual fields especially is helpful to predict the success or failure

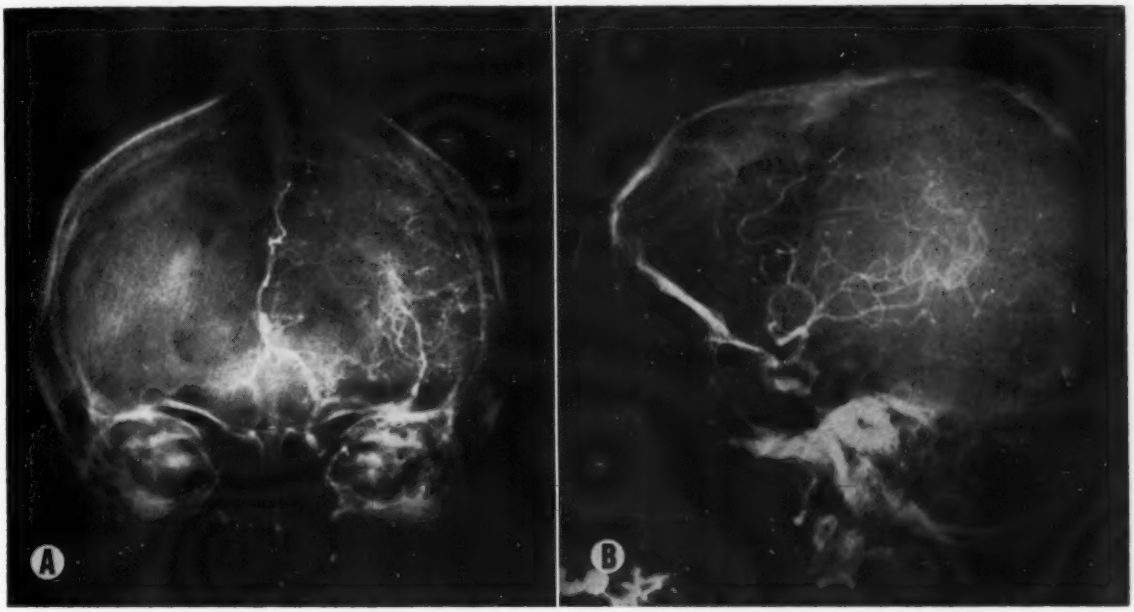

Fig. 7. Tuberculum Sellae Meningioma. The proximal portion of the left anterior cerebral artery is sharply elevated from its usual transverse position in frontal view (*A*) and from the normal oblique position in lateral view (*B*). The frontal view of the right carotid angiogram appeared as a mirror image of the left, which indicated that the lesion was midline in position and bounded by the internal carotid arteries, the anterior cerebral arteries and the anterior communicating artery. The detection of bitemporal hemianopia led to use of the correct procedure for roentgenologic diagnosis and subsequently to surgical therapy. (See Fig. 6.)

of angiographic diagnosis. Visual defects which denote a lesion at the optic chiasm suggest the presence of a process more amenable to diagnosis by carotid angiography than defects which indicate an abnormality of the optic radiations. The close relation of the optic radiations to the lateral ventricles makes ventriculography a more consistently valuable procedure to diagnose the cause of homonymous hemianopia.

4. Gross displacement of the calcified pineal gland backward, downward or lateralward in plain head roentgenograms usually indicates a tumor suitable for angiographic localization. Anterior displacement of the pineal and displacement of the choroid plexus often foretell the failure of carotid angiography.

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RUPTURE OF AN ANEURYSM OF THE INTERNAL CAROTID ARTERY DURING CEREBRAL ANGIOGRAPHY

CASE REPORT

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IT HAS now become a rather common practice to do early cerebral angiography following intracranial bleeding. In general it is considered a valuable and safe procedure.[1,2,3] We are reporting this case because of the unusual roentgenographic studies obtained, and also because of the early fatality following the angiography.

REPORT OF CASE

E.W., female, aged forty-nine, had had periodic headaches for many years. In the last week of September, 1952, she had a very severe headache, as well as a stiff neck. This persisted for several days before gradually improving. The headache returned on October 2, 1952, and was improving, when on the evening of October 4, 1952, the patient collapsed. She became cyanotic and comatose immediately and was taken to a hospital, where lumbar puncture was done, revealing blood in the spinal fluid. After several days she became more alert and was transferred to St. Luke's Hospital on October 7, 1952, for cerebral angiography. She was rational but complained of severe headache and stiff neck. There were no specific neurological findings.

Under general anesthesia the patient was intubated and the left internal carotid artery was injected percutaneously with 8 cc. portions of 35 per cent diodrast, for lateral and anteroposterior views of the cerebral arterial vascular pattern. Four different placements of the needle in the arteries of the right side of the neck with subsequent injections of the contrast medium filled only the external carotid artery. On the fifth attempt the internal carotid was finally injected. Immediately following this injection the patient became apneic and the pulse rose to approximately 200 per minute. Blood pressure dropped to 80/50. The anesthetist gave immediate artificial respiration for ten minutes, following which there was spontaneous breathing of the Cheyne-Stokes type. The blood pressure rose to 130/80 and then to 140/100. The pulse rate dropped to 100 within the next half hour. These abnormalities disappeared and the patient was returned to her room, with a pulse of 92, respiration 18, and blood pressure 130/78, but still comatose. In the hours which followed, the temperature rose to 103.4°F. and there were some convulsive movements of both arms and legs with rectal and vesical incontinence. Twenty-four hours after the arteriogram, respirations were deep and regular. The blood pressure and pulse were normal. Spontaneous swallowing and spontaneous movements of all four extremities occurred. Dilatation of the right pupil and ptosis of the right upper eyelid

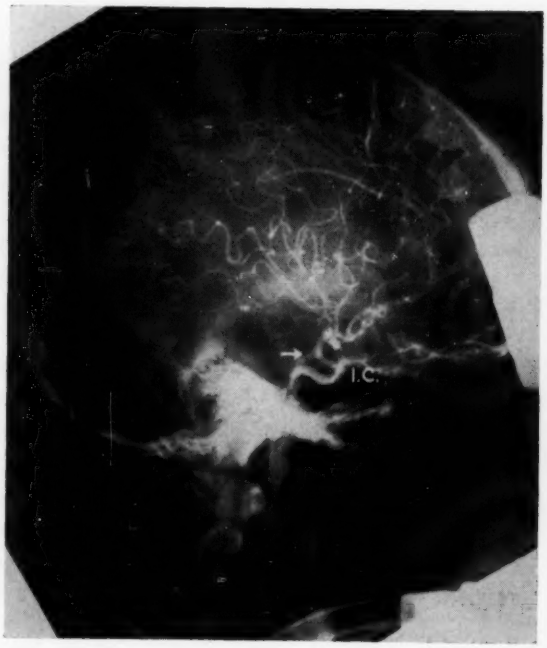

FIG. 1. Patient E.W. Left internal carotid arteriogram showing aneurysmal bulge of the vessel just above the clinoid process. (Film reversed for comparison on right side.) I.C. = internal carotid artery.

was noted at this time. After thirty hours had elapsed the patient became cyanotic. Respirations dropped to 12 per minute and finally ceased. Death occurred thirty-two hours postoperatively. Unfortunately a postmortem examination was refused.

Films taken after left carotid injection show a normal cerebral arterial pattern, except for a small outpouching on the posterior aspect of the internal carotid, projecting posteriorly toward the posterior clinoids (Fig. 1). The anteroposterior films show no abnormality and contrast medium is seen to have crossed over the anterior communicating artery into the right anterior cerebral artery. The single film taken after right internal carotid injection shows marked narrowing and irregularity of the internal carotid artery opposite the sixth cervical vertebra (that is, just above the bifurcation of the right common carotid artery). The artery can be traced through a normal course up to the anterior clinoid process. At this point the continuity is lost. The contrast medium is seen outside the normal cerebral vascular tree. It can then be followed posteriorly along the clivus from which

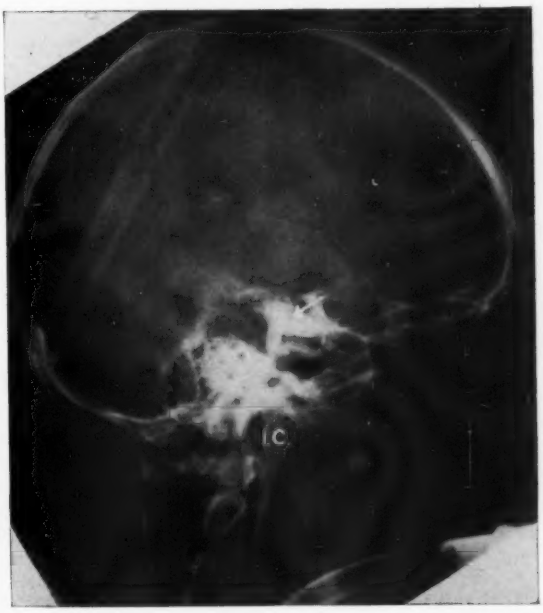

Fig. 2. Patient E.W. Right internal arteriogram showing extravasation of the contrast material out of the internal carotid into the basilar cisterns and under the pons. (Note lack of vessels of basilar group.) I.C. = internal carotid artery. Arrow points to extravasation of contrast material.

Fig. 3. Patient E.W. Right external carotid arteriogram showing the region of the sella. S.T. = superficial temporal artery. E.C. = external carotid artery.

it is separated by a thin parallel clear area down to the region of the foramen magnum (Fig. 2).

The significance of the bulge on the left internal carotid artery is not definite, but from its position below the origin of the anterior cerebral artery it would appear to be an aneurysm of the internal carotid artery. This is probably the most common site of aneurysm of this artery.

The difficulty in obtaining the right internal carotid angiogram is readily explained on the basis of the marked narrowing at its origin. The irregular contours are characteristic of arteriosclerotic changes which occur at this site with great frequency. The peculiar configuration of the extravasated medium can only be explained by assuming that it lies in the subarachnoid cisterns under the brain stem.

Figure 3 shows the right external carotid circulation in this patient just prior to the internal carotid injection on the same side. It is apparent that the region of the cistern is empty of contrast material. For comparison with a normal vascular structure in this region Figure 4 is included. This was made on another patient by injection into the vertebral artery. It shows the basilar artery, with diodrast passing through the posterior communicating artery and thence in a retrograde manner filling the

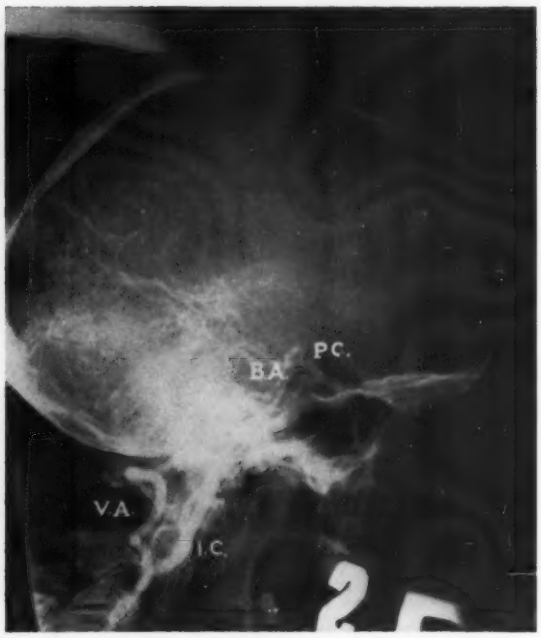

FIG. 4. Vertebral arteriogram (Patient E.R.), used for comparison, showing retrograde passage of contrast material into the internal carotid artery. V.A. = Vertebral artery. I.C. = Internal carotid artery. B.A. = Basilar artery. P.C. = Posterior communicating artery.

internal carotid artery. The tubular character of the basilar artery and its divergence from the clivus is well illustrated in contrast to the situation in Figure 2. It appears evident that the contrast material extravasated through a break in the internal carotid artery probably at the site of an aneurysm. The pupillary dilatation and other signs of third motor nerve palsy which were observed after angiography would be compatible with the expansion of such an aneurysm. The procedure of angiography in this patient appears to have been responsible for the concomitant rupture of the aneurysm.

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Vol. 71, No. 6

THE STUDY OF MITRAL REGURGITATION BY ROENTGEN KYMOGRAPHY

WITH OBSERVATIONS ON THE MOVEMENT OF CARDIAC CALCIFICATIONS

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C. LIAN, working in François Franck's laboratory in 1908,[21] and Wiggers and Feil, in 1922,[43] demonstrated in dogs with experimentally produced mitral regurgitation that, as one might predict, ballooning of the left atrium occurs during ventricular systole. In man the same phenomenon has been observed in a variety of ways. Occasionally it has been observed directly as a visible pulsation of a mammoth left atrium presenting to the right of the sternum.[3]* In occasional cases the carina, widened and elevated by the enlarged left atrium, has been seen to pulsate on bronchoscopy.[3] Atrial expansion has been detected indirectly by balloon tracings from the esophagus,[13,21] by roentgenoscopic observation of the barium-filled esophagus,[7,20] by the Ruggles cinematograph as used years ago by Chamberlain and Dock,[2] by electrokymographic studies of the left atrium[5,8,22,24,26,34,35] and by roentgen kymography.[14,19,31,32,36,37] It is with the last technique that we are concerned here since it appears to be the best method we have for objective demonstration of the phenomenon.

Direct roentgenoscopic observation of the barium-filled esophagus has simplicity to recommend it. However, timing of the movements and rough grading of their amplitude is difficult for the most expert roentgenoscopist and well-nigh impossible for one who only occasionally roentgenoscopes these patients. The esophageal balloon technique for demonstrating atrial pulsations is difficult and the tracings have been of small and inconstant form. A recently reported[18] improved technique is promising. The presence of overlying arterial structures as well as difficulties in exactly localizing at roentgenoscopy the left atrial portion of the cardiovascular shadow always casts doubt on electrokymographically recorded "left atrial pulsations."[34] Roentgen kymography largely avoids these difficulties and has the advantage of at least rough quantitation.

It is difficult to know who first applied the roentgen kymographic method to the demonstration of systolic expansion of the left atrium. About simultaneously studies were made in Germany,[19,29] France,[31,32] and this country.[14]

The main portion (posterior wall) of the left atrium is normally inaccessible to ordinary roentgenographic study since it is not in contiguity with lung.[39] There are three general methods for roentgen kymographic demonstration of mitral regurgitation, or better, three methods for outlining a substantial portion of the left atrial wall for roentgenographic study:

(1) Barium filling of the esophagus represents the most useful and perhaps the most "natural" method.

(2) Occasionally the left atrium presents far over on the right heart border and is outlined by lung tissue.[3] Less frequently the enlargement is into the left hemithorax (see Fig. 7).

* In 1901 Owen and Fenton[29] described a case of mammoth left atrium in which a "pulsation, synchronous with that of the heart, was felt over the right front of the chest, from the second space to the seventh vertically, and laterally from the mid-axillary line to within an inch of the sternum. A systolic thrill was felt in the right infra-mammary region." A trocar and cannula, "the size of a goose quill," inserted in the right mid-axillary line for thoracentesis inadvertently entered the huge left atrium. Although Ewart saw the patient and although aortic aneurysm was suspected, no exact diagnosis was arrived at before autopsy which revealed that the left atrium had an estimated capacity of 30 ounces. The mitral orifice admitted four fingers and was obviously incompetent.

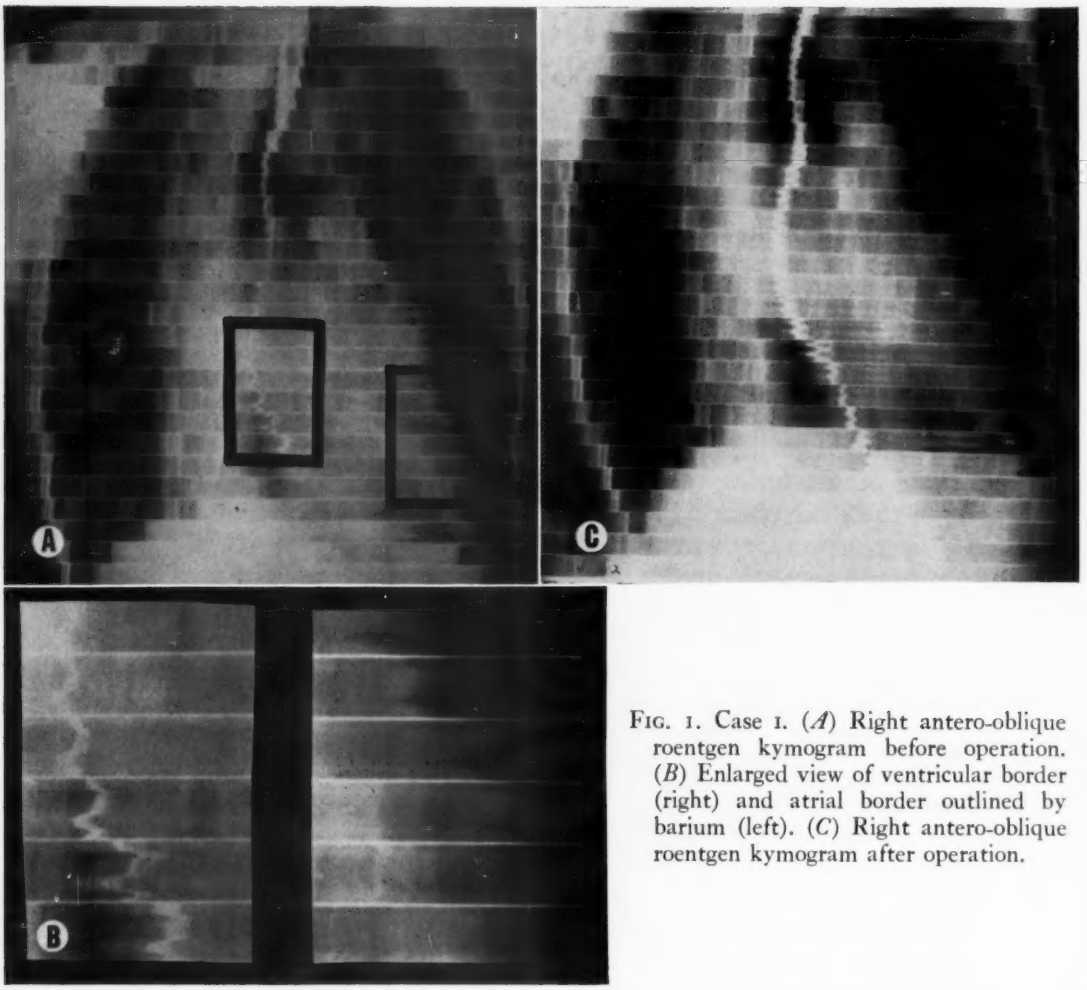

FIG. 1. Case 1. (*A*) Right antero-oblique roentgen kymogram before operation. (*B*) Enlarged view of ventricular border (right) and atrial border outlined by barium (left). (*C*) Right antero-oblique roentgen kymogram after operation.

(3) Occasionally calcification[28,33,47] occurs in a portion of the wall of the left atrium (in either a portion involved by a MacCallum patch,[25] a portion which bears the main brunt of the regurgitant stream, or a portion with a mural thrombus). In this situation the left atrium provides its own contrast medium for kymographic study.

The specific roentgen kymographic finding in mitral regurgitation is an outward movement of the left atrial wall (as outlined by barium, calcium, or air-filled lung) synchronous with the inward movement (ejection phase) of the ventricle. This outward movement of the atrial wall begins slightly before the onset of the main mediad movement of the ventricular border since regurgitation has its onset during the isometric contraction phase of the ventricle. A plateau pattern has been described as characteristic. However, the plateau may be inapparent at faster cardiac rates. The important feature of the pattern is the outward movement of the atrial wall early in ventricular systole.

ILLUSTRATIVE CASES

Barium-Filled Esophagus and Right Antero-oblique Projection.

CASE 1. H.W.T. This patient had characteristic physical signs of mitral stenosis and "insufficiency." The mitral systolic murmur was classified as Grade 1, however, and it was believed clinically that the patient approached the state of "pure mitral stenosis." Figure 1*A* is a

roentgen kymogram taken in the right antero-oblique position with barium in the esophagus.* As is seen more clearly in Figure 1*B*, there is an outward movement of the left atrial wall synchronous with inward movement of the opposite ventricular border.

Finger-fracture of a calcified mitral valve was performed with marked diminution in the diastolic murmur, perhaps some increase in the systolic. The roentgen kymogram (Fig. 1*C*) was taken two and one-half years after operation. At this time the patient demonstrated a Grade II systolic murmur at the apex. Ordinary chest films demonstrated further enlargement of the left atrium which could now be seen projecting on the right heart border. There was now more evidence of regurgitation than in the preoperative film.

Case II. T.P. (J.H.H. 573214) was a white man, aged thirty-nine, who had chorea and acute rheumatic fever in childhood. Nocturnal dyspnea with blood spitting and fever developed two years before being seen here. There was typical accentuation of the first mitral sound and an opening mitral "snap." At the apex there was a faint Grade I systolic murmur and a loud typical diastolic rumble with accompanying thrill. The roentgen kymogram (Fig. 2) shows systolic expansion waves on the part of the barium column in contact with the left atrium. These are not of large amplitude, however. Inward movement with atrial systole is clearly indicated preceding the outward movement with ventricular systole. Also demonstrated is moving calcium in the mitral valve and (less well seen) in the aortic valve. The mitral valve cusps show large amplitude movements which are in phase with the atrial border movements. The aortic valve, on the other hand, shows movement opposite in direction to that in the atrial border.

At operation the surgeon reported that one could feel "moderate regurgitation" through the stenotic valve. Roentgen kymograms were repeated eleven months after valvulotomy. They were technically excellent. Suffice it to say that for practical purposes no mitral regurgitation could now be demonstrated by roentgen kymography. It was of interest that the movements of the calcified mitral cusps were now of even larger amplitude than previously.

* As in reading most articles dealing with roentgen kymography, a magnifying glass is useful for studying the illustrations.

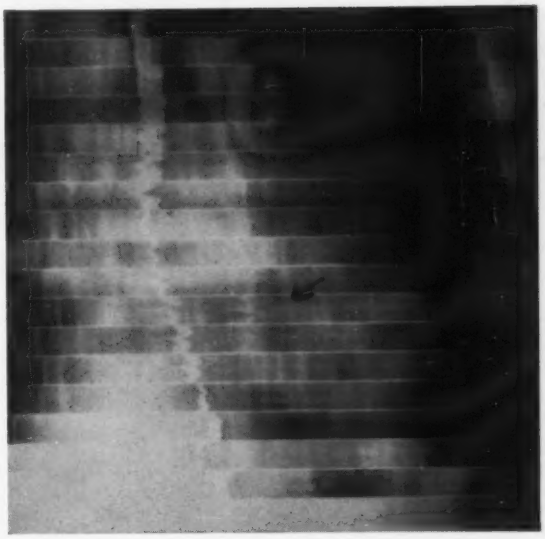

Fig. 2. Case II. Right antero-oblique roentgen kymogram before operation. Mitral valve calcification indicated by arrow.

Barium-Filled Esophagus and Posteroanterior Projection.

Case III. M.P. (J.H.H. 562308) was a white woman, aged twenty-eight who developed rheumatic fever following scarlet fever. She had signs of mitral stenosis and "insufficiency;" the signs of "insufficiency" were the more striking. In fact, the characteristic diastolic rumble of stenosis was frequently inaudible. Figure 3*A* presents a roentgen kymogram in the posteroanterior projection with barium in the esophagus. The esophagus is displaced to the right and shows pulsation in that direction synchronous with the mediad movement of the ventricular segment of the left heart border. It is somewhat unusual to be able to demonstrate clearly the esophageal movement in the posteroanterior projection as seen here. In this patient the left auricle is also visible on the right heart border and its pulsations are demonstrated (less well than on the esophagus) against the contrast of the lung.

Soon after the study illustrated in Figure 3*A* mitral valvulotomy was performed by Dr. Alfred Blalock. It was the operator's impression that there was no evidence of mitral regurgitation. (Blood pressure was 80/60 mm. Hg during operation as compared to 110/65 before operation.) Furthermore, in spite of the absence of an unequivocal murmur of mitral stenosis, the valve opening was among the smallest Dr.

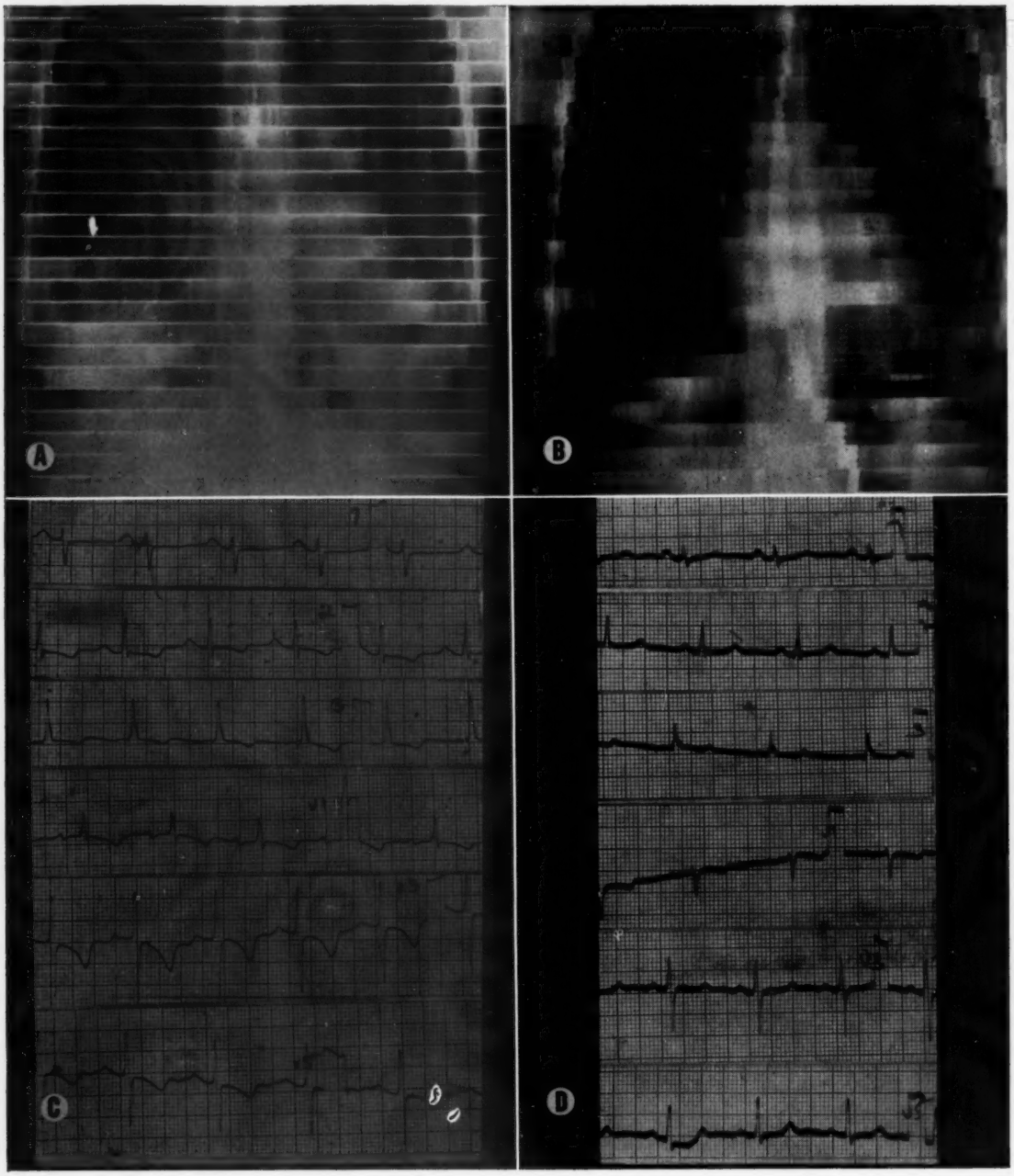

FIG. 3. Case III. (*A*) Posteroanterior roentgen kymogram before operation. (*B*) Posteroanterior roentgen kymogram after operation. (*C*) Electrocardiogram before operation. (*D*) Electrocardiogram after operation.

Blalock had seen. There appeared to be some regurgitation after finger-fracture at the commissures. Results were exceedingly gratifying. Exercise tolerance increased from a state of severe limitation to one permitting essentially normal activity. When examined six months after operation the patient looked and acted like a normal person. There was now a "classical" diastolic rumble located in protodiastole and presystole but the systolic murmur had greatly diminished and might be classified as Grade 1 at the most. Heart size had decreased to normal. The electrocardiogram (Fig. 3*C*) which had previously shown right axis devia-

tion and right ventricular hypertrophy and "strain" was now within normal limits (Fig. 3*D*). Of great interest is the roentgen kymogram (Fig. 3*B*) which in addition to showing the reduction in heart size also demonstrated essentially no evidence of mitral regurgitation. (Although only the posteroanterior view is shown for sake of comparison with the preoperative film, lateral and both oblique roentgen kymograms likewise showed no significant regurgitation.) This may represent an objective demonstration that the operation for mitral stenosis may help the "insufficiency," too, by allowing the cusps to coapse more efficiently. The absence of a typical mitral stenosis murmur may have been the result of the exceptionally small orifice present; it is more difficult to reconcile the roentgen kymographic finding with the surgeon's impression.

Case iv. M.Pf. (J.H.H. 445263) was a white woman, aged thirty-four with an unusually strong family history of rheumatic heart disease. She had never had frank rheumatic fever but at the age of twenty-nine began to have attacks of dyspnea and cough which was often productive of frothy, bloody sputum. There were typical signs and symptoms of mitral stenosis and "insufficiency." Auricular fibrillation had developed at the time the roentgen kymograms (Fig. 4) were made. With barium in the esophagus positive systolic waves of large amplitude are demonstrable in both the posteroanterior (Fig. 4*A*) and the right antero-oblique (Fig. 4*B*) projection. The relative simplicity of this pattern as compared with that in many of the other illustrations is probably the result of auricular fibrillation. The additional features produced by organized contraction of the atrium in sinus rhythm are not present. Operation was decided against because it was felt there was probably too large an element of mitral regurgitation.

Lung as Contrast. Right Lung.

Case v. M.B. (J.H.H. 566346) was a white woman, aged thirty-eight who had several attacks of acute rheumatic fever beginning at the age of nine years. She had obvious physical

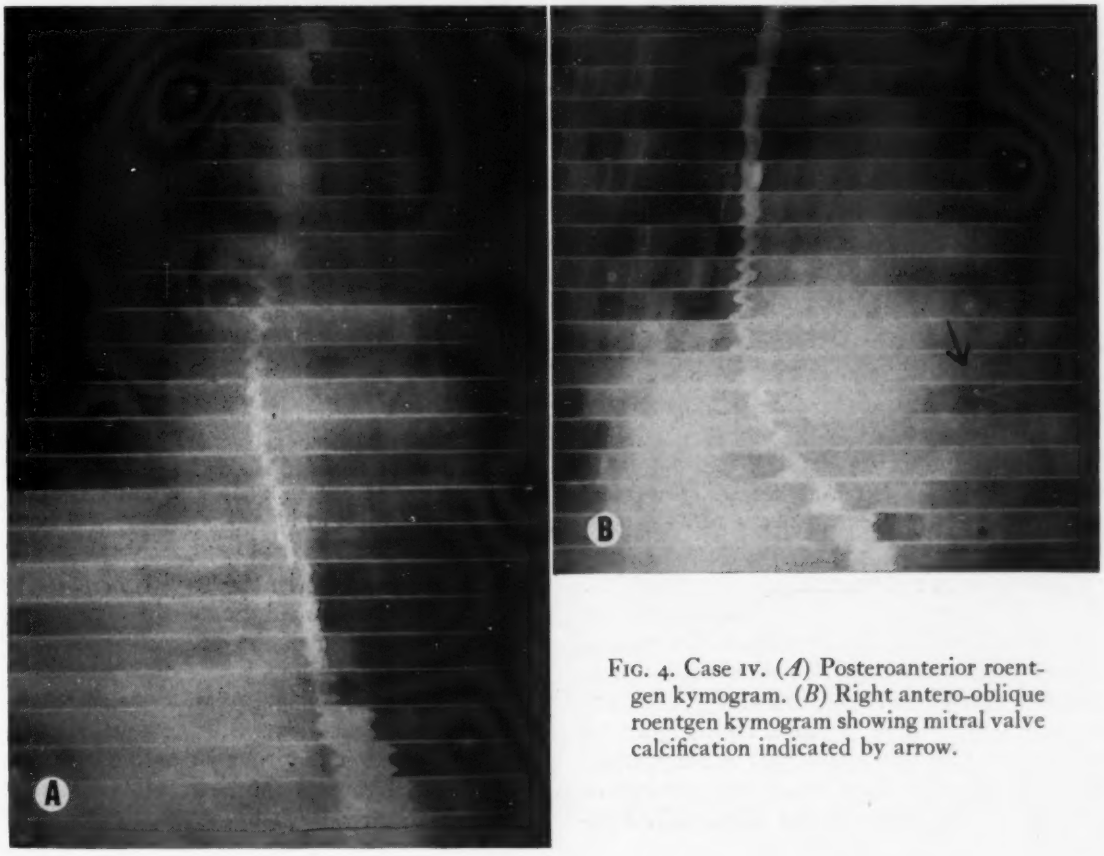

Fig. 4. Case iv. (*A*) Posteroanterior roentgen kymogram. (*B*) Right antero-oblique roentgen kymogram showing mitral valve calcification indicated by arrow.

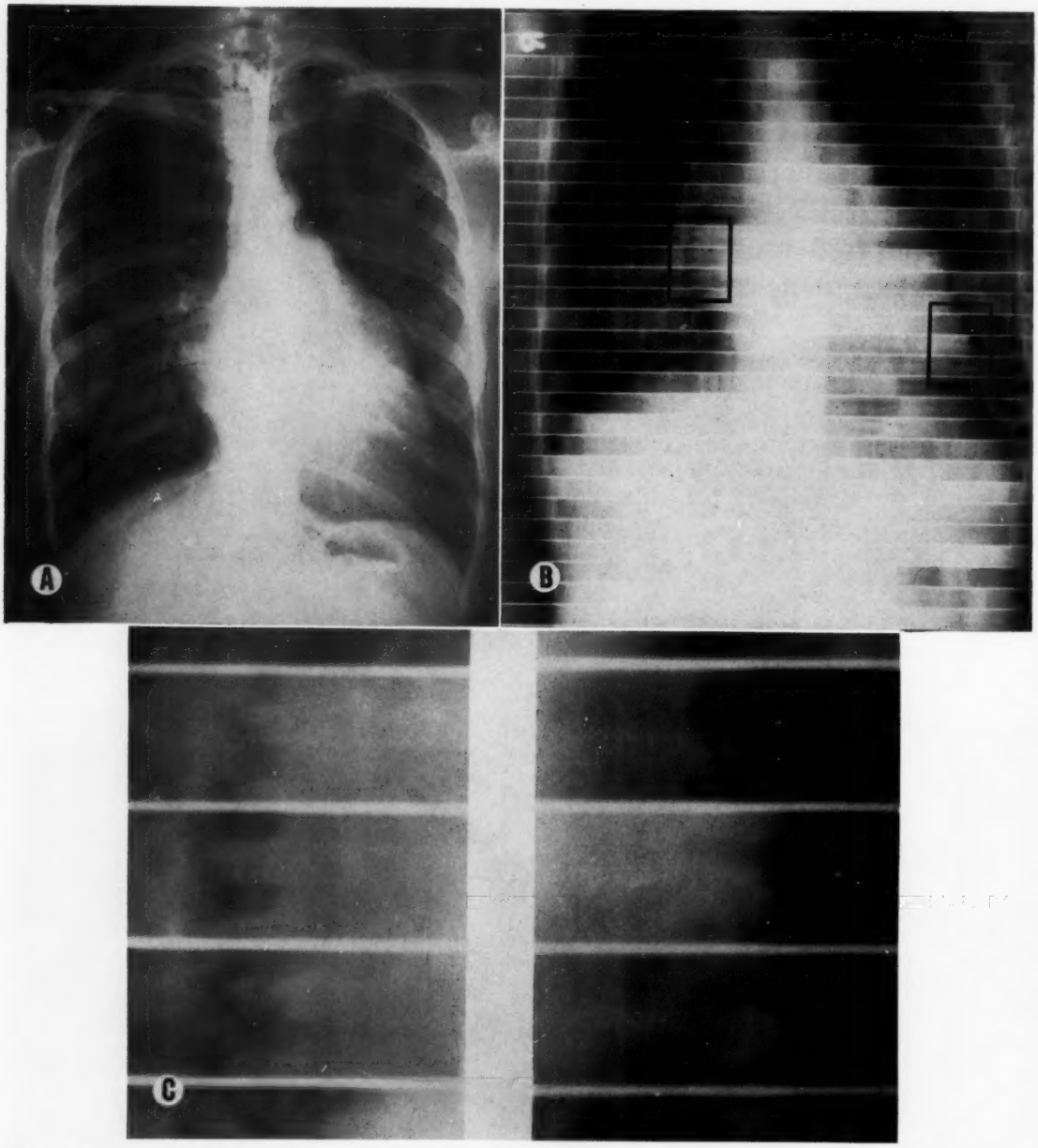

Fig. 5. Case v. (*A*) Posteroanterior roentgenogram. (*B*) Posteroanterior roentgen kymogram. (*C*) Enlarged view of ventricular border (right) and atrial border outlined by lung (left).

signs of both mitral stenois and regurgitation. The systolic murmur was estimated as Grade IV or V, the diastolic as Grade II or III. On cardiac catheterization resting pulmonary artery pressure was high normal (35/16 mm. Hg), capillary pressure slightly high (19 mm. Hg). Figure 5*B* represents a roentgen kymogram in the posteroanterior projection. The left atrium presents as a bulge on the right border (Fig. 5*A*). Synchronous with ventricular systole its wall shows a systolic outward movement of greater amplitude than that of the ventricular border as visualized in this plane. It was surprising how little compression, displacement, or *movement* of the esophagus was demonstrable in this patient. The main regurgitant jet would appear to be directed toward the right axilla. Partly because of the roentgen kymographic demon-

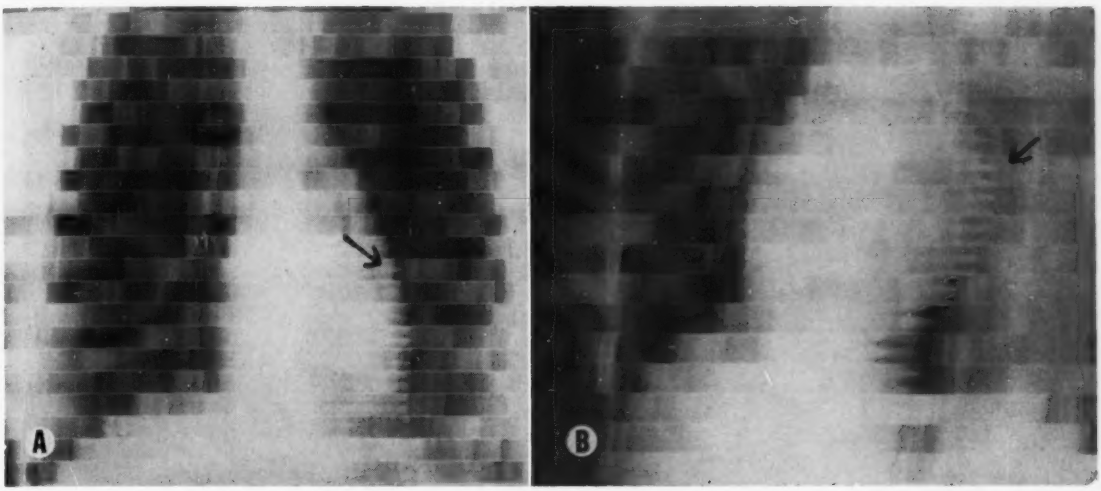

Fig. 6. Case vi (*A*) Posteroanterior roentgen kymogram. (*B*) Left antero-oblique roentgen kymogram. In each case the area demonstrating systolic expansion of the atrium is indicated by an arrow.

stration the patient was judged to have too much mitral regurgitation to make surgery for the stenotic element of her disease likely to attain beneficial results. As in Case iv this judgment may have to be revised in the light of experience with cases such as that of patient M.P. (Case iii) above.

Lung as Contrast. Left Lung.

Case vi. E.H. (J.H.H. 452300) was treated here in 1947 for acute staphylococcal endocarditis, engrafted, it is thought, on rheumatic mitral valvulitis. By physical signs there was only mitral regurgitation, no stenosis. Repeatedly, on roentgenoscopy, a prominent systolic expansion was visible at the upper limit of the left ventricular border. Even aneurysm of the left ventricle was suggested as a possibility. In Figure 6 the arrows indicate the area of systolic expansion in roentgen kymograms in the posteroanterior and left antero-oblique projections. It is the left atrial wall which is involved in the anomalous movement. In the posteroanterior projection it may be the auricular appendage which is visualized. Furthermore, it is of interest that the barium swallow in this patient revealed minimal compression with no displacement of the esophagus and very litttle movement; the mechanics of this situation—perhaps as a result of the cusp principally eroded by the infection—appears to be such as to produce effects almost exclusively on the left wall of the atrium. This case provides an interesting contrast with Case v, in which the regurgitant jet appears to be directed mainly in the direction of the right axilla.

Recently at this hospital a patient with

Fig. 7. This patient, a white woman, aged forty-four, with rheumatic disease of the mitral valve, demonstrates a mammoth left atrium bulging into the left hemithorax.

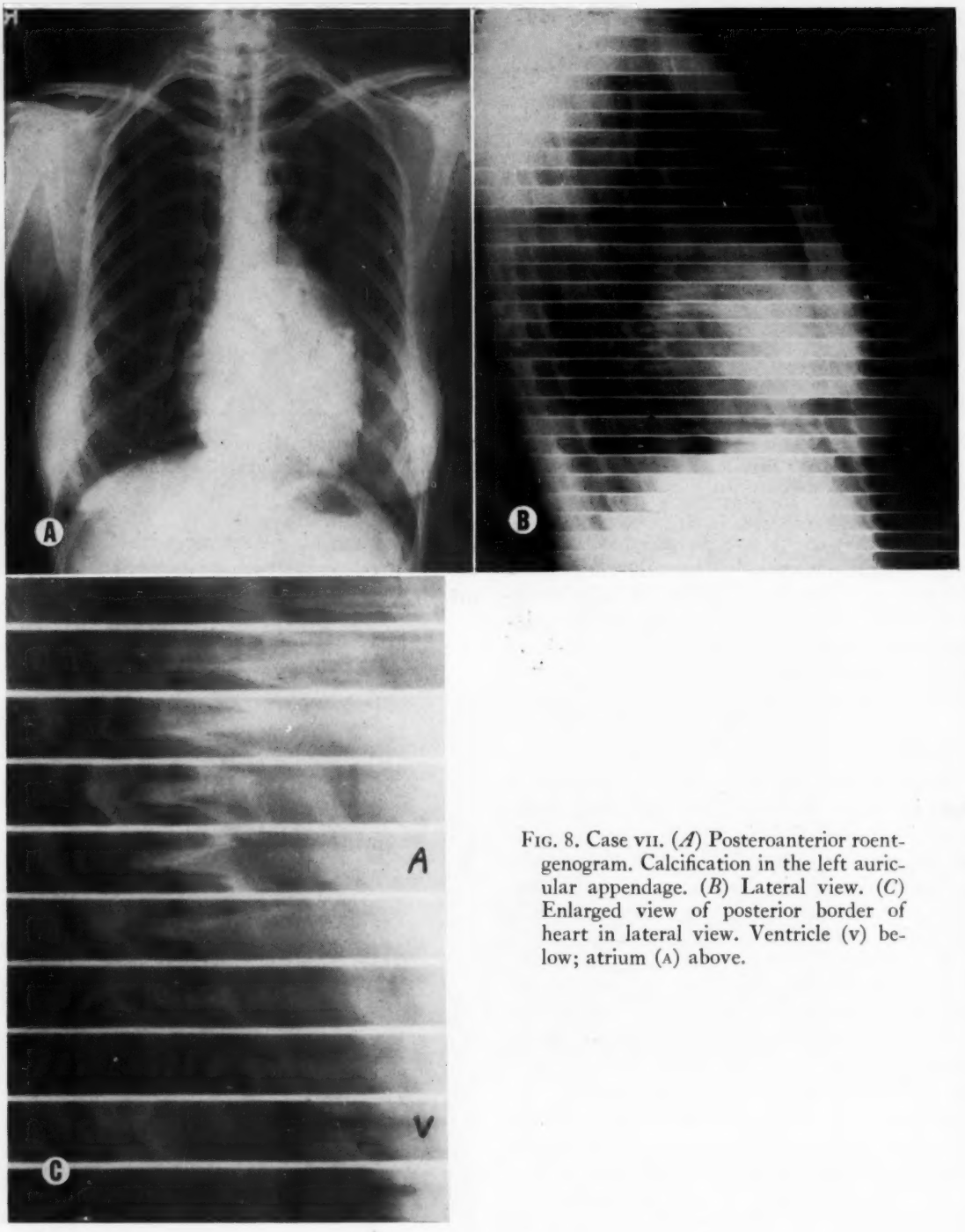

FIG. 8. Case VII. (*A*) Posteroanterior roentgenogram. Calcification in the left auricular appendage. (*B*) Lateral view. (*C*) Enlarged view of posterior border of heart in lateral view. Ventricle (V) below; atrium (A) above.

mitral regurgitation has been studied (J.H.H. 597532) in whom a mammoth left atrium presented far over into the left hemithorax* rather than into the right as is the more usual case (Fig. 7). Such a case may represent a more advanced form of the same hemodynamic set-up present in Case VI.

* This patient died late in 1953. Necropsy confirmed the roentgenologic impressions.

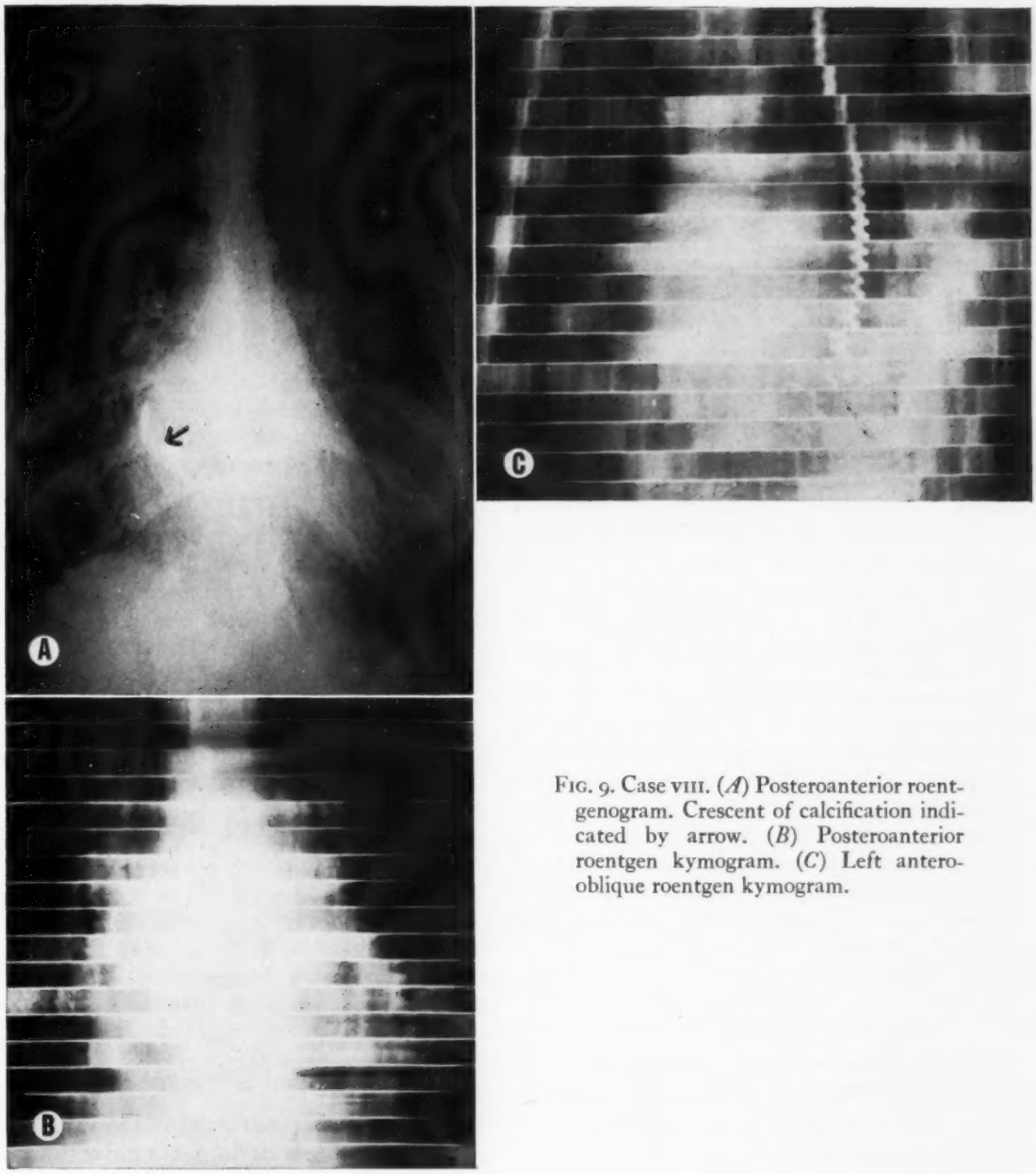

Fig. 9. Case VIII. (*A*) Posteroanterior roentgenogram. Crescent of calcification indicated by arrow. (*B*) Posteroanterior roentgen kymogram. (*C*) Left anterooblique roentgen kymogram.

Calcification of the Atrial Wall.

Case VII. P.M. (J.H.H. 559979), a white woman aged twenty-seven, gave a history of rheumatic fever following scarlet fever with several recurrences thereafter. She had a Grade IV mitral systolic murmur; a diastolic murmur has been heard only questionably. The posteroanterior roentgenogram of the chest (Fig. 8*A*) reveals a heart of "mitral configuration" with calcification in the mid-portion of the left heart border. This calcification appears to lie in the left auricular appendage and showed leftward movements of small amplitude with ventricular systole. The entire posterior wall of the left auricle is extensively calcified and it reveals on lateral roentgen kymograms systolic expansions of large amplitude (Fig. 8*B*). Fortunate for timing's sake, ventricle (probably

the left) appears in silhouette below the atrium. In the enlarged view (Fig. 8*C*) a clear indentation precedes the large systolic outward movement of the atrial wall. This represents the contraction of the atrium itself immediately preceding the ventricular contraction with its resultant regurgitation into the atrium. (The patient had normal sinus rhythm.) The excellence of roentgen kymograms in demonstrating calcification is illustrated by the fact that ordinary lateral films of the chest did not reveal the calcium seen so clearly by roentgen kymography.

Case viii. P.B. (J.H.H. 513441) was a white woman aged thirty-four who had had several episodes of frank rheumatic fever and in whom the diagnosis of mitral stenosis was made at the age of twenty-three. No definite systolic murmur was audible at the apex but there was a very loud and typical rasping diastolic murmur. Mitral valvulotomy was attempted but entry into the atrium was impossible because of the presence of much thrombus and because of the fact that the auricular appendage was reduced to a mere nubbin. Figure 9*A* shows the crescent of calcification in the right border of the left atrium. In the posteroanterior roentgen kymogram (Fig. 9*B*) the calcified area shows lateralward movements of small amplitude with ventricular systole. Figure 9*C* is a reproduction of a roentgen kymogram in the left antero-oblique projection. This was the view which showed systolic expansion components of the greatest amplitude. The importance of complete studies is illustrated.

FURTHER ILLUSTRATIVE CASES

In the following cases reproductions of roentgen kymograms are not included because they showed little or no evidence of mitral regurgitation.

Case ix. S.O'N. (J.H.H. 616116) was a white woman aged twenty-seven, in whom the roentgen kymograms appear to corroborate the clinical impression of "pure" mitral stenosis. She had had essentially no symptoms. The first mitral sound was greatly accentuated with a palpable shock; there was no apical murmur in systole; there was a very loud, long, typical diastolic rumble with presystolic build-up. Roentgen kymograms with the esophagus filled with barium showed no significant positive systolic components and they are interpreted as showing no evidence of mitral regurgitation.

Case x. J.B. (J.H.H. 617335) was a white man, aged forty-six, who likewise had very little disability which can be related to his heart. For over thirteen years he had been known to have an apical systolic murmur. Examination revealed moderate cardiac enlargement and a loud systolic murmur transmitted to the axilla and back and accompanied by a systolic thrill. Although a high degree of mitral regurgitation might have been expected, roentgen kymograms with the esophagus filled with barium revealed only slight evidence of same. The left atrium was only slightly enlarged. The roentgen kymographic findings were believed to be consistent with the usual inaccuracy of murmur intensity for the diagnosis, much more the quantitation, of mitral regurgitation.

Case xi. E.S. (J.H.H. 349124) was a white woman, aged thirty-six, who was studied two months after mitral valvulotomy. At that time there was evidence of rheumatic activity with fever. In addition, there was a prominent, apparently expansile, systolic pulsation of the liver. Roentgen kymograms with the esophagus filled with barium showed no evidence of mitral regurgitation. Although no roentgen kymographic studies were performed before operation the surgeon reported a regurgitant jet of moderate size; it may be that this finding represents amelioration of mitral regurgitation as in Case iii. On the other hand, on the right heart border and low on the esophageal border in right antero-oblique position, where the right atrium is likely to be represented, there were systolic expansion waves which were interpreted as evidence of considerable tricuspid regurgitation.

DISCUSSION OF TECHNIQUE

The technique for roentgen kymographic study of the left atrium should take the following considerations into account:

(1) For sake of approximate uniformity in the films the length of exposure should be varied inversely with the heart rate. In the many cases with atrial fibrillation this is, of course, impossible to do with exactitude. There is commercially available* a device in the form of a rotating vane which records on each film the duration of the kymographic exposure by the number of

* Liebel-Flarsheim Company, 303 West Third Street, Cincinnati 2, Ohio.

rotations of the vane which occurred in each exposure. This provides a ready means of estimating the length of the heart cycle and the approximate heart rate at the time of the study.

(2) When, as will most frequently be the case, barium filling of the esophagus is used, the degree of obliquity (right antero-oblique) employed should be such that good ventricular pulsations are visualized on the border opposite the left atrium. This usually requires a somewhat lesser degree of rotation than that employed for standard right antero-oblique roentgenograms.

(3) The penetration should represent a compromise between that necessary to produce sharp detail of the barium outline, on the one hand, and the less sharply contrasted ventricular border, on the other hand.

(4) Complete studies should be done. By and large, the right antero-oblique view will be most useful but, as is well demonstrated by the examples cited above, postero-anterior, left antero-oblique and lateral views should be taken and may give additional information of value. The precise nature of the mitral valvular defect, and, as a result thereof, the direction of the regurgitant stream is variable. One is never surprised by the appearance of regurgitation waves in some projections and not in others. One lateral projection appears to have no advantage over the other.[16]

(5) In the interpretation, comparison of corresponding portions of the ventricular and atrial patterns may be facilitated by the use of tracing paper (*i.e.*, one can trace the patterns one below the other) or of calipers (with which, for instance, one can time on an atrial frame the point where ventricular ejection begins).

ATTEMPTS AT QUANTITATION

For the sake of a rough mathematical estimate of regurgitant volume the enlarged left atrium might be considered as a hemisphere and the increment in volume occurring with mitral regurgitation can be conceived of as portrayed in the sketch in Figure 10.

Fixation at points A and B, corresponding, perhaps, to the annulus fibrosus mitralis, is assumed.

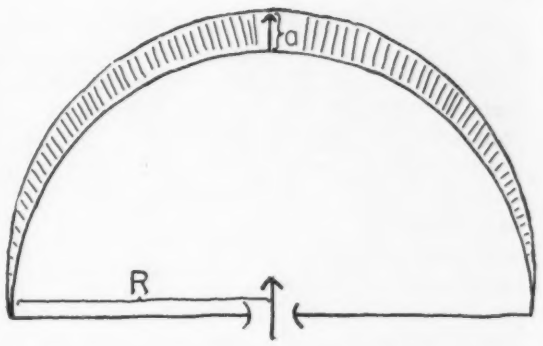

FIG. 10. Diagrammatic representation of left atrium and of its change with regurgitation. The last formula is an approximation arrived at by discarding terms 2 and 3 of the first formula which in this application are negligibly small.

Whereas the resting figure is a hemisphere, the figure after regurgitation is a truncated sphere. That expansion of the left atrium in regurgitation is not symmetrical but comes closer to the pattern illustrated in the sketch is suggested by the anatomical situation which prevents expansion toward the ventricle and probably also toward the right atrium. It is also suggested by the actual roentgen kymographic observation of a maximum movement in one or two frames with falling off of the measurements in frames on both sides in that projection, say a view of the barium-outlined border, and falling off also in other demonstrations of expansion, say the lung-outlined border.

The formula for the increment volume which is shaded in the sketch and which may be termed "estimated regurgitant volume" is as follows:

$$E.R.V. = \pi/6(6ar^2 + 3a^2r + a^3)$$

r = "resting" radius;
a = maximum increment.

In this application a is almost always a fraction of 1 centimeter and becomes negligibly small when raised to a higher power as in the second and third terms of the formula. Therefore, the formula can be simplified to the following:

$$E.R.V. = \pi ar^2.*$$

This formula has been utilized in the calculations in Table 1. The value used for a was the largest amplitude of outward movement of the atrial border recorded in any projection by any of the three methods of outlining the atrium.

The radius of the hemisphere is estimated from a

* That this is the formula for a cylinder can be considered a coincidence.

posteroanterior film of the chest. In the patients with enlarged left atria a moderately "hard" film usually provides sufficiently sharp outlines of the left atrium to permit an estimate of the transverse dimension in the frontal plane. Since the value for the radius is cubed, small variations in the estimation of the transverse dimension result in large variations in the estimated atrial volume (compare this volume in Cases VII and VIII). This is unfortunate for the accuracy of this method. When angiocardiographic data on the dimensions of the left atrium are available, these may be employed.

In general, the estimates of the volume of these enlarged left atria are within the expected range. The left atrium in normal adults has a volume of 30 to 40 cubic centimeters.* The smallest volume in this group occurred in Case VI in whom left atrial enlargement was relatively slight. The largest volume was about a pint (Case V), by no means an incredible figure.

The values given for maximum amplitude of border movement are the values used for a (largest increment) in the formula for regurgitant volume. A value for estimated regurgitant volume is arrived at by use of the simplified formula, πar^2, given above.

The values for regurgitant volume estimated in Table I are consistent with general clinical estimates. Furthermore, they are of the same order of magnitude as mathematical estimates derived by other means.[11,17] Using these other methods (which also have sources of inaccuracy) the maximum regurgitant volumes observed have equalled the aortic flow. This is roughly true also in the case of the mathematical estimates given here.

It seems likely that the normal left atrium *cannot* be treated as a hemisphere. I would emphasize that this treatment is approximately valid *only* in the enlarged atrium which may well be flattened to a hemisphere on the back of the heart.

This approach is not intended to be definitive. Its inaccuracies are obvious. It is merely intended as an exploratory attack on the problem of quantitation. The main value of these estimates lies in the demonstration that the regurgitant volume so arrived at is of reasonable order of magnitude. If there were better methods for determining the dimensions of the left atrium, estimations of regurgitant volume by the roentgen kymographic method would probably be more reliable.

CRITIQUE OF THE METHOD

Both positive and negative errors may occur in the evaluation of mitral regurgitation by roentgen kymography. There are the following bits of evidence suggesting positive errors:

(1) In patients with calcification of the mitral cusps (and mitral stenosis) (see

* This estimate of the volume of the normal left atrium was arrived at by measurements in autopsy hearts. Before opening the heart all pulmonary veins were tied off close to the atrium except one to which a clamp was applied. An opening into the left ventricle was made. The heart was then inverted and the left atrium filled with saline in a retrograde direction through the mitral orifice. The clamp was then removed from a pulmonary vein and the fluid collected and measured. The atrium of normal size is free to assume a shape closer to that of a sphere. In the case of mammoth left atrium, of which there was no representative in this group, there is probably also large error if this type of treatment is applied. It should be noted that this method for calculating regurgitant volume requires that only that portion of the atrium which actually participates in systolic expansion approximate a hemisphere in shape.

TABLE I

Case No.	r = Estimated Frontal Radius of Left Atrium	Estimated Volume of Left Atrium (as hemisphere) $1/2(4/3\pi r^3)$	a = Maximum Amplitude of Border Movement			Estimated Regurgitant Volume = πar^2
			Barium	Lung	Calcium	
	cm.	cc.	mm.	mm.	mm.	cc.
I Preop.	4.5	197	3.0			19
Postop.	5.0	262	4.5	2.5		35
II Preop.	4.0	134	3.0			15
Postop.	3.5	90	0			0
III Preop.	5.0	262	4.0			31
Postop.	4.0	134	0			0
IV	5.25	304	5.0	2.5		43
V	6.0	452	4.0			45
VI	3.25	72		6.0		20
VII	5.0	262			12	94
VIII	5.25	304	4.0		2	35

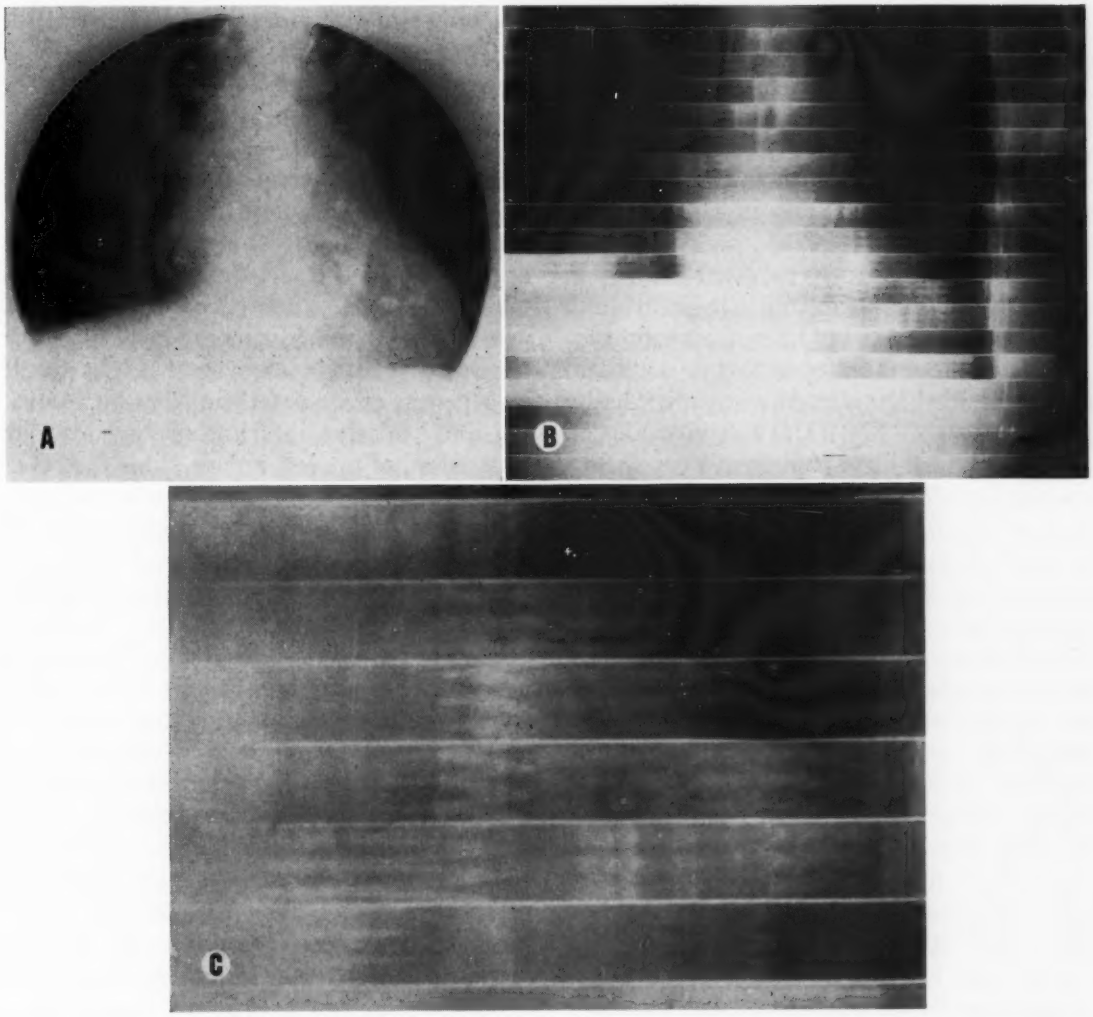

Fig. 11. This patient, a white woman, aged eighty-eight, had had rheumatic fever in childhood. (*A*) This view taken with an exposure time of 1/60 second demonstrates the calcified annulus fibrosus mitralis. (*B*) This roentgen kymogram demonstrates that the ventricular border and the base of the heart as outlined by the calcified mitral ring move toward each other during ventricular systole. The movement of the base of the heart is of large amplitude.

Cases I, II and IV) the calcified structures show in ventricular systole dextro-postero-craniad movements which follow the same direction and timing as the movement of the esophageal border and have an amplitude approximating or even exceeding that of the esophageal motion. (Postoperatively Case II showed large amplitude movements of the mitral calcifications without evidence of regurgitation.) In 6 patients with calcific mitral stenosis Froment and colleagues[9] made the same observation. In a single case of presumed *cusp* calcification Wolferth and Margolies[44] observed movements in the ventricular direction with ventricular systole.

The statement has been made[6] that this atrium-ward direction of movement in mitral stenosis is opposite to the normal direction. Actually the valve cusps normally bulge into the atrium with ventricular systole.[4] Confusion has arisen from failure to differentiate movement of the base of the heart including the annulus fibrosus

mitralis from movement of the mitral cusps. Normally the mitral ring and base of the heart do descend with ventricular systole as demonstrated centuries ago by Leonardo da Vinci and more recently by observations of cases with calcified annulus mitralis[38] and of animals in which radiopaque markers were placed on the heart.[42] Figures 10*A* and 10*B* represent studies in an eighty-eight year old white woman (J.H.H. 481084) who had a history suggestive of rheumatic fever in childhood and had a calcified annulus fibrosus mitralis by roentgenogram (Fig. 11*A*) but virtually no functional disability. Roentgen kymograms revealed no evidence of mitral regurgitation of the barium-filled esophagus. They showed (Fig. 11*B*) movement of the calcified mitral ring toward the ventricle with ventricular systole. (Although this patient had no roentgen kymographic evidence of mitral regurgitation there was a rasping apical systolic murmur. The question might be raised whether creaking of the calcified fibrous skeleton of the heart might have participated in the production of this murmur.)

Study of a case of mitral stenosis with calcified annulus might be very instructive. The calcifications which show movement in cases such as those described here are believed to be in the valve cusp but may be located in the base of the valve and follow the movement of the muscular base of the heart. It is difficult to imagine that a rigid stenotic valve could bulge enough to produce the large amplitude movements displayed by these cases, but such would appear to be the situation.

(1) The normal atrium-ward bulging of the mitral cusps may be responsible for retropulsion of an enlarged atrium. This retropulsion would be falsely interpreted as evidence of mitral regurgitation. In addition, it has been suggested that the base of the heart may show a trium-ward movement with systole, opposite in direction to the normal one. Even a decrease or elimination of the ventricle-ward movement would remove the canceling effect of the opposite directions of movement of the valve cusps and the valve seating. With several-fold increase in the volume of the atrium it may be that its weight prevents or reduces the normal downward systolic movement of the base of the heart. If such were so—and complete proof is lacking—the ventricle might operate more like an appendage of the left atrium than is normally the case. Peristence of the normal movement of the cardiac apex toward the base with ventricular systole might result in a piston effect producing systolic retropulsion, falsely interpreted as systolic expansion, of the left atrium.

(2) Calculations of regurgitant volume, using expansion measurements derived from roentgen kymograms and estimates of atrial volume, have given impossibly high values in some hands using methods other than those applied here. This is not a very strong argument against the validity of the roentgen kymographic method as an index of regurgitation since it may just as well be that the mathematical treatment used was inappropriate.

(3) A third bit of evidence of positive error derives from the cases in which regurgitation was believed to be present by roentgen kymography but could not be demonstrated at autopsy or at operation. Froment and his associates[9] described a case of mitral stenosis in which roentgenologically there was "indisputable" systolic expansion of the left atrium. Yet at autopsy the valve proved to be perfectly competent when tested for water tightness by the method these authors have described.[10] Case III, described above, likewise showed a striking discrepancy between the roentgen kymographic findings and the surgeon's palpatory impression. Although some writers question its accuracy,[45] most seem to agree that the surgeon's impression is a valid index of mitral regurgitation if one makes certain that systemic blood pressure is at the usual level at the time the observation is being made.[7,23] The Peter Bent Brigham Hospital group[7] found "expansion of the auricle" roentgenoscopically in 29

patients, in only 14 of whom was a regurgitant jet felt by the surgeon. Reservations as to the accuracy of the surgeon's estimate of regurgitation at the operating table are in order. A forceful jet representing a relatively small regurgitant volume may impress him more than a regurgitant stream with less velocity but of much greater volume.

What might be the cause of a false positive sign of mitral regurgitation? Piston action of the left ventricle, as already mentioned, is one of the more likely causes. That the retropulsion is the result of right ventricular hypertrophy[7] may be partially excluded by the failure to find the sign in cor pulmonale.[26] That the movement is transmitted[7] from the right atrium which shows expansion from tricuspid insufficiency can be excluded by the absence of primary roentgen kymographic evidence of tricuspid insufficiency (*i.e.*, absence of systolic expansion in the right auricle). Furthermore, Case x, described briefly above, had marked clinical and roentgen kymographic evidence of tricuspid regurgitation without evidence on either score of mitral regurgitation. Rapid flow of blood into the left atrium in early systole due to pulmonary venous hypertension and relaxation of the left atrium may be a factor in the positive systolic waves observed.

Factors possibly responsible for errors in the negative direction are even harder to evaluate than the positive errors. Decrease in the normal flexibility and elasticity of the atrial wall and extensive thrombus formation might be expected to decrease the systolic expansion phenomenon. By and large, the negative errors are theoretical ones only and it must be uncommon for significant regurgitation to be present with failure of properly taken roentgen kymograms to demonstrate "systolic expansion." The largest errors appear to be in the positive direction. Of course, in a mammoth left atrium the systolic expansion may be inapparent; that is, the regurgitant blood effects little change in the radial dimension of the chamber.[3]

The great handicap to evaluation of any method for measuring mitral regurgitation is that there is *no* method sufficiently above suspicion for use as a standard of reference. It is the current feeling of the writer that the method discussed here does provide a useful indication of regurgitant volume for the physician or radiologist who familiarizes himself with the technique.

It is true that the roentgen kymographic diagnosis of mitral regurgitation is fraught with theoretical difficulties. Yet no single method will make the diagnosis and most are more difficult than this. The systolic murmur is notoriously unreliable, having itself both positive and negative error. In one study, roentgenoscopic observation of left atrial systolic expansion showed a better correlation with the surgeon's impression of regurgitation than did the presence or absence of systolic murmur.[7] The results of the roentgen kymographic examination must be considered in clinical context. When present, this sign strengthens other suspicions of mitral regurgitation such as one or more of the following: little or no accentuation of the first mitral sound, absence of an opening mitral snap, enlargement of the left ventricle (even slight), marked enlargement of the left atrium.[6] Recently, Brigden and Leatham[1] have reported that, in all 25 patients in whom the total clinical picture (and in 4 cases necropsy) indicated mitral regurgitation and in whom the sign was searched for, systolic expansion of the left atrium was demonstrated roentgenographically.

An Ancillary Roentgen Kymographic Technique for the Study of Mitral Leak. In 1936 Hirsch and Gubner[15] suggested that the left ventricular border might show a quite different pattern of movement in mitral insufficiency as opposed to mitral stenosis. In mitral stenosis, filling is likely to be slow. In mitral insufficiency, ventricular filling is likely to be abnormally rapid as a result of the free atrioventricular communication together with the high left atrial pressure produced by the regurgitation of the previous ventricular systole. The au-

thors illustrate the particular pattern of left ventricular movement which is likely to occur when one of these lesions is present in predominant and striking degree. Note should certainly be made of the shape of the diastolic phase of left ventricular border movement and this information correlated with that provided by the left atrial border movement. It must be recalled that aortic regurgitation may produce rapid ventricular filling with a pattern somewhat like that in mitral leak.

Tricuspid Insufficiency. A few words about the roentgen kymographic signs of tricuspid regurgitation are pertinent here. Such regurgitation is most often functional, *i.e.*, due to dilation of the right ventricle. The same systolic expansion may be demonstrated on the right atrial border and provides the clinician with information as to the effects of the mitral disease on the right heart. No additional films need be taken since the right atrium should be outlined in some of the films taken for study of the left atrium. Hepatic pulsation can be recorded on the diaphragm by vertical roentgen kymograms in full inspiration. By close observations of timing relationships these studies may help the differentiation of systolic liver pulsations from the presystolic pulsations[12] of atrial septal defect, cor pulmonale, tricuspid stenosis, constrictive pericarditis,[41] etc.

Valve Calcification. The examples given (Fig. 2 and 4*B*) demonstrate the usefulness of this method in the demonstration of valve calcification. Calcification is often demonstrated by roentgen kymograms when it is not by other types of roentgen examinations.[30] Furthermore, the type of movement may assist in the identification of the shadow as valve calcification. The roentgen kymogram may permit, by the direction of the movement demonstrated, a differentiation of mitral and aortic calcification—the aortic calcifications, as a rule, show movements toward the ventricle in the first portion of ventricular systole—and of annulus fibrosus calcification from valve calcification. Wynn[46] has the impression that significant mitral incompetence occurs twice as commonly in patients with gross mitral calcification.

Comment. Experience with the two conditions which the author has studied by this technique—constrictive pericarditis[27] and mitral regurgitation—convince him that roentgen kymography, when thoughtfully applied, can give worthwhile information in the realm of pathological physiology. Exception must be taken to a recent statement[40] that "with the possible exception of ventricular aneurysm, there are no pathognomonic kymographic patterns."

SUMMARY AND CONCLUSIONS

By specific illustrations it has been shown that the left atrium can be outlined for study of mitral regurgitation by the barium-filled esophagus, by air-containing lung, or by calcification in the atrial wall itself. Details of the technique and potentialities of the method are discussed and a critique of the results presented. A case is presented (Case III) in which virtual disappearance of pronounced roentgen kymographic evidence of mitral regurgitation followed mitral valvulotomy. Case II demonstrates roentgen kymographic evidences of the same course of events in somewhat less dramatic fashion.

It is pointed out that other factors than mitral regurgitation alone may be responsible in part for the production of the outward movement of the atrial wall in systole. The evaluation of the roentgen kymographic method for estimating mitral regurgitation is difficult in the absence of any completely reliable method to provide a basis of reference. In general, however, when considered in clinical context, roentgen kymograms provide worth while aid in the evaluation of the factor of regurgitation in mitral valve disease.

Included are cases illustrating "pure" mitral stenosis (Case IX), the inadequacy of auscultation as a gauge of mitral insufficiency (Case X) and the additional feature of tricuspid regurgitation (Case X).

Calcified heart valves are well demon-

strated by roentgen kymography. The movement of the mitral valve calcifications is in the direction of the atrium during most of ventricular systole. On the other hand, the base of the ventricle as visualized by calcification of the annulus fibrosus mitralis moves in the direction of the ventricle ("descends") during ventricular systole.

Also presented is an example of an unusual situation: rheumatic disease of the mitral valve with massive dilatation of the left atrium into the *left* hemithorax.

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FISSURES IN BILIARY CALCULI

FURTHER OBSERVATIONS

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IN A previous publication[2] the author discussed the presence of and the nature of gas-containing fissures in certain biliary calculi. The high incidence of such fissures in calculi stored for several years was stressed, but the need for further investigation of such fissures has been manifested in the writings prior to and subsequent to our earlier effort.

Unquestionably the finding of gas-containing calculi upon roentgenological examination of the patient is rare, but is this because fissures are rare or because they are difficult to demonstrate? What is the actual incidence of fissures in calculi at the time of operation? Do most fissures contain gas or do they contain something else such as bile? Does the fluid environment influence fissuring or is the latter merely a phenomenon of ageing? What kinds of calculi tend to fissure? What is the explanation for the gas sometimes found in the fissures? Does the gas cause the fissures? Are calculi permeable to gases and liquids? All of these questions naturally occur and it is our purpose to try to answer some of them after describing our observations and simple experiments.

Material Used:

The surgically removed gallstones of 100 consecutive cholecystectomy patients were studied in a standardized manner with the following exceptions:

(a) Solitary calculi were excluded.

(b) Calculi averaging less than 3 mm. in diameter were excluded.

(c) Ductal calculi were excluded.

Standard Procedure (Experiment 1)

1. A roentgenogram was made of the removed gallbladder before opening.
2. The organ was opened and the calculi were described and classified grossly.
3. Twenty representative calculi were selected for use in the "environment experiment" described below. When fewer than twenty calculi were present, they were all used in the study.
4. A roentgenogram was made of the fresh calculi in air.
5. Five calculi were placed in each of the following containers in order to expose them to artificial environmental conditions
   Container A. Air at room temperature
   Container B. 95 per cent alcohol
   Container C. Normal saline
   Container D. 10 per cent formalin
6. The calculi were removed from their artificial environments and immediate roentgenograms were made in air. Those from solutions B, C, and D were wet while those from A were dry. The duration of exposure to the A, B, C, and D environments was variable, since the calculi were placed in them while fresh (ranging from July, 1950, to December, 1951) and they were all removed on the same day (November 1, 1952).
7. The calculi were fastened to cards (preserving the A, B, C, and D groupings) and were allowed to dry in air at room temperature for one month, after which roentgenograms were again made.
8. The three roentgenograms of the same calculi (*i.e.*, a, fresh, b, after exposure to artificial media, c, dried in air) were studied and compared.

Explanatory Note:

One thousand three hundred and four calculi from 100 patients were studied in the manner outlined above. For statistical purposes, however, we have considered all the calculi removed from a given host as a unit. Any patient having one or more fissured calculi was considered positive for

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fissuring. Our figures therefore indicate how many different patients had fissured calculi—not how many individual calculi contained fissures. The findings in fresh and stored as well as wet and dry calculi are listed in Table 1.

Are Fissures Actually Rare? From Table 1 it can be seen that fissures are very common. In calculi freshly removed from the gallbladder, fissures were recognized in 48 per cent of patients. After the calculi were dried either immediately or after storage in fluid, fissures were seen in 57 per cent of patients.

The increased incidence of fissures after drying suggests that additional fissures may have formed during the period of observation. However, it is more likely that the fissures were merely more obvious after drying. On review we could find no convincing evidence that new fissures formed during the period of storage in fluid environments.

In the fresh wet calculi, the fissures were usually filled with fluid. The latter was readily identified, expecially in stones of low density, since the fluid was more dense than the calculus, and was seen as a plane or star of increased density. The typical appearance is illustrated in Figure 1 which shows the same calculi before and after drying.

In a number of instances the dense stars could be seen while the calculi were still in the intact gallbladder, and frequently they could be seen when immersed in 5 cm. of water. Three intact gallbladders are shown in Figure 2. The fissures are clearly visible.

In the calculi of some patients both gas-containing and fluid-containing fissures were found to co-exist. An example is shown in Figure 3. This is interesting inasmuch as it indicates that the basic factor is the presence of the fissure, rather than the contents of the fissure. The contents which may be fluid, gaseous or semisolid, will be discussed below.

The Effect of Drying. When the biliary calculi in Experiment 1 were allowed to remain in air they quickly became dry on the surface. As the drying process continued, fluid was lost from within the calculus. This could be appreciated by the study of serial roentgenograms and by weighing. In those calculi containing fluid-filled fissures (roentgenologically determined) there was loss of fluid and replacement with gas. This exchange obviously indicates that fluid and gases can pass through the substance of gallstones. The change in appearance is illustrated in Figure 1. There is convincing evidence that drying was associated with widening of the fissures already present. Gross widening could usually be

TABLE I

INCIDENCE OF FISSURING IN 100 CHOLECYSTECTOMY PATIENTS HAVING MULTIPLE CALCULI

(Recognition Based Upon Roentgenograms)

I. Fresh (Removed surgically July, 1950–December, 1951)	
Total patients having recognizably fissured calculi—48	
Of these:	
Fissures contained fluid in	40 patients
Fissures contained gas in	15 patients
Fisures contained fluid and gas in	7 patients
II. After 1–2½ years in environments of saline and formalin	
Number of patients having recognizably fissured calculi before drying—48	
(Same distribution of fluid and gas as in fresh calculi above)	
III. After 1–2½ years in environments of air (group A) and alcohol (group B)	
A. Fissures were found in the calculi of	57 patients
B. Fissures were found in the calculi of	20 patients
(See text for solvent action of alcohol)	
IV. After removal from fluids and drying in air	
Fissures were recognized in the calculi of	57 patients
Fissures contained fluid in	0 patients
Fissures contained gas in	57 patients

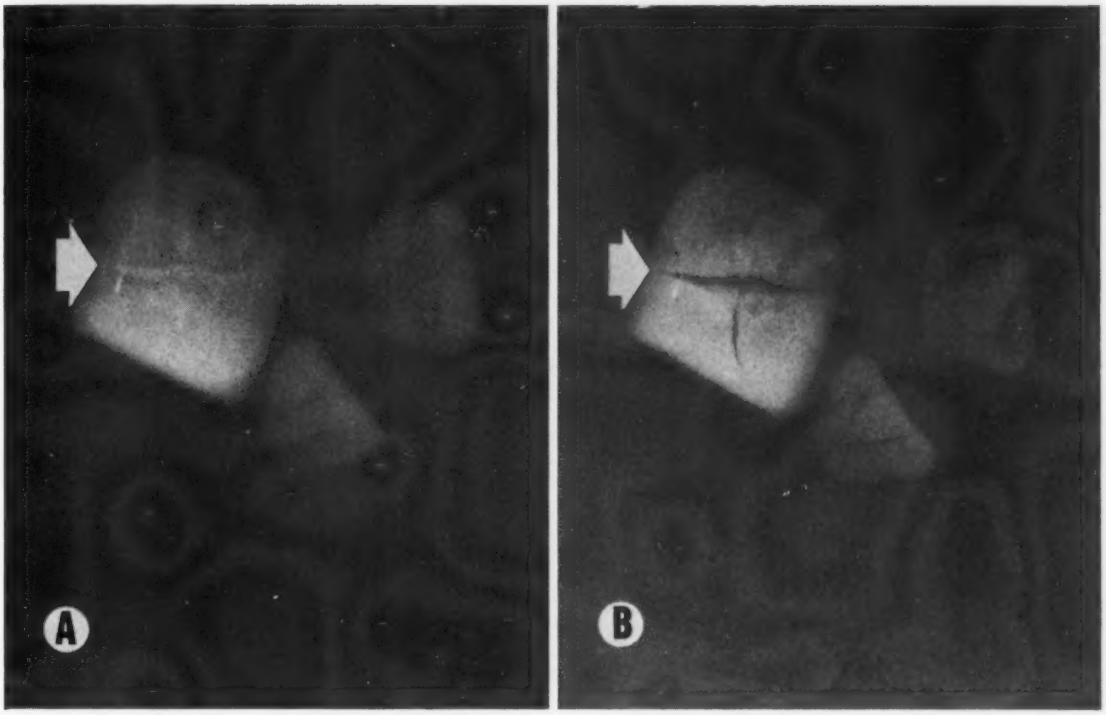

Fig. 1. *Fluid in Fissures of Fresh Gallstones.* (*A*) Roentgenograms of three nonopaque calculi in air. Arrow indicates fluid-filled fissures running transversely and vertically in the largest calculus. (*B*) Identical projections after drying. The same fissures now contain gas which can also be seen in the smaller calculi.

appreciated roentgenologically in two or three weeks, but after six seeks no further widening was recognized. The widening phenomenon is presumably the result of dehydration and colloid-crystalloid shrinkage. It is illustrated in Figure 4. During this drying period a number of calculi underwent spontaneous fragmentation.

How Long Does the Fluid Remain in the Fissures? (Experiment 2) In order to determine the length of time required for the fluid in the fissures to evaporate under normal atmospheric conditions, ten patient-units of calculi which were known to have fluid-filled fissures were examined roentgenologically daily until the fluid could no longer be seen and the fissures appeared to contain only gas.

Findings: Some small calculi of the nonopaque variety lost their fluid in twenty-four hours. Most of the calculi measuring between 3 and 10 mm. in diameter were free of fluid in five days. A number of calculi from 10 to 30 mm. in diameter required twelve days for complete drying. The time required appeared to be influenced not only by the size but also by the porosity of the outer shell.

Effect of Storage in Artificial Fluid Environments for from One to Two and One-Half Years. When this experiment was planned it was anticipated that the nature and concentration of the environmental fluid would probably influence the formation of fissuring in the various groups of calculi. Normal saline was used to determine whether or not the incidence of fissuring could be decreased. Formaldehyde is a hardening agent and it was expected to hasten or augment the formation of fissures. Alcohol was selected because it is a dehydrating agent and it was also expected to dissolve excess surface crusts.

Observations: Physiological saline and 10 per cent formalin (solutions C and D) exerted no recognizable influence upon the incidence, type, or extent of the fissures.

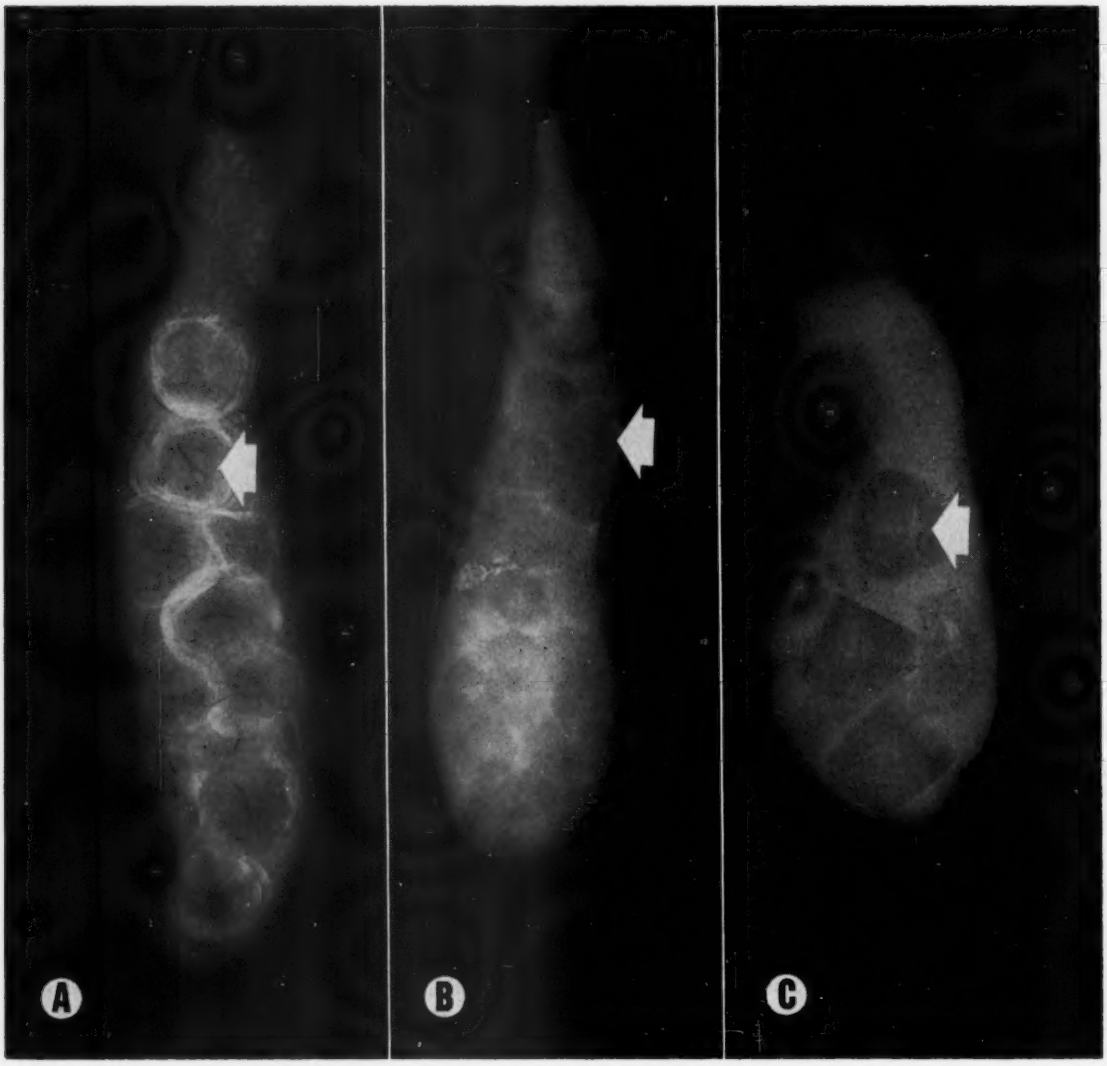

FIG. 2. *Fissures in Unopened Gallbladders.* Roentgenograms of three intact surgically removed gallbladders. In (*A*) the calculi are opaque and many contain gas-filled fissures. In (*B*) and (*C*) the calculi are of less than bile density and the fluid-filled fissures are relatively dense. Arrows indicate the typical stellate fluid collections.

We were unable to find convincing proof that any new fissures formed during the time the calculi were in solutions C and D. Some fissures seemed to become slightly wider, but this change was minimal.

It was difficult to evaluate the effect of 95 per cent alcohol since the dehydrating effect was more than offset by the solvent action of the alcohol. Not only was the outer crust dissolved, but also most of the smaller mulberry calculi dissolved completely. In calculi of firm composition, existing fissures were obscured or obliterated in the alcoholic environment. This unforeseen effect was attributed to the powerful solvent action of the reagent. Even after drying, the fissures which had previously existed failed to reappear. A typical patient-unit of calculi is illustrated in Figure 5. Here fissures can be seen in the calculi stored in A (air), in C (saline), and in D (formalin), but the B group (alcohol) is homogeneous and unfissured.

Diffusion of Gases Through Calculi. (Experiment 3) We have previously suggested[2] that naturally occurring internal shrink-

age creates "voids" or "faults" of negative pressure within calculi. In an attempt to equalize the pressure, fluids or gases dissolved in the surrounding bile diffuse into the negative pressure voids. It seemed desirable to determine whether a gas could be diffused through a calculus while surrounded by a fluid. We could not fabricate an artificial zone of negative pressure inside a calculus in order to investigate this phenomenon. We, did, however, carry out a simple related experiment using a negative pressure pump.

A dried nonopaque calculus 13 mm. in diameter which was known to contain a central gas-filled fissure was placed in a flask of boiled water. (The water was boiled to remove dissolved atmospheric gases.) The calculus was seen to float. A layer of mineral oil was placed above the calculus to act as a seal from atmospheric air. The calculus was so buoyant that almost one-third of it projected above the level of the water (Fig. 6*A*).

The flask was tightly stoppered and a negative pressure pump was attached which provided a constant negative pressure of 10 pounds per square inch. This was maintained for thirty minutes. After twenty minutes of negative pressure the calculus was noted to be floating much deeper in the water, and after thirty minutes it sank to

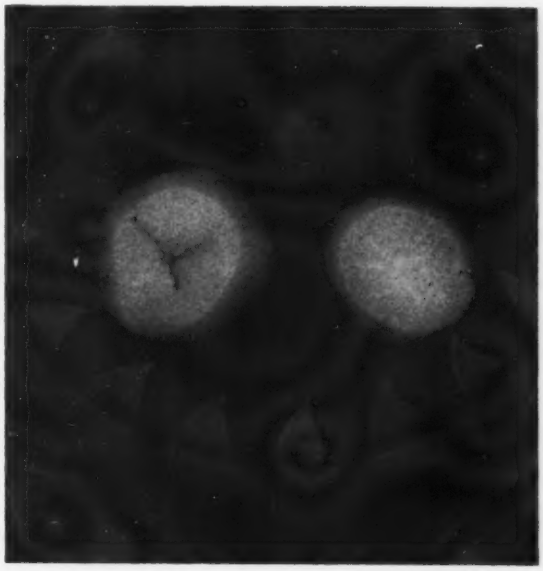

Fig. 3. *Fissures Containing Gas and Fluid in the Same Gallbladder.* Roentgenograms of several biliary calculi freshly removed from the same gallbladder. The fissures of the large calculus on the left contain gas. The companion stone on the right has its fissures filled with fluid.

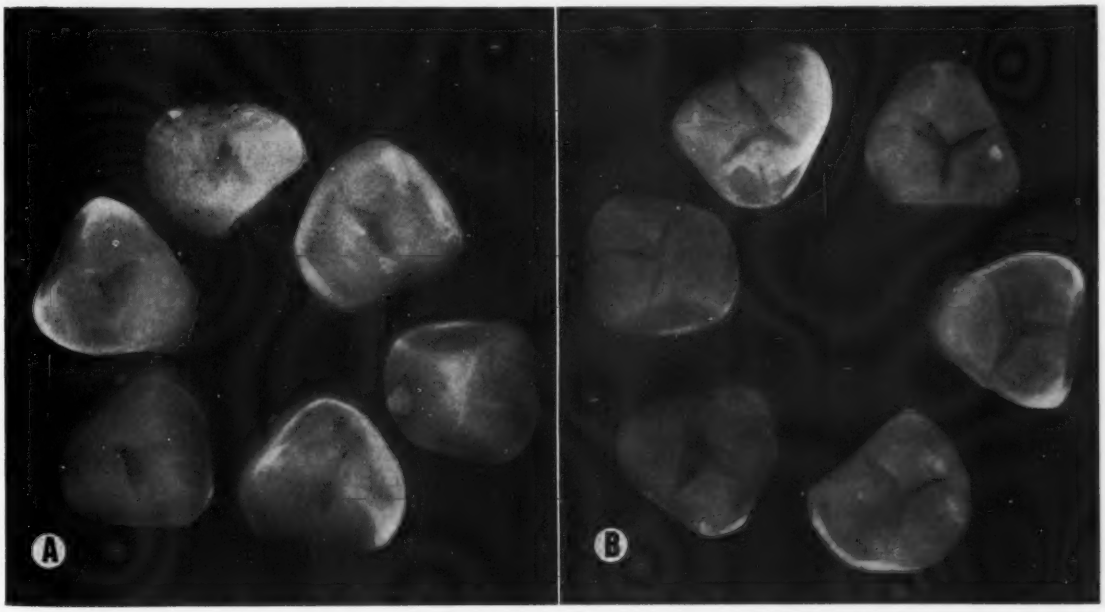

Fig. 4. *Shrinkage Resulting From Drying.* Roentgenograms of six large biliary calculi. In (*A*) they are freshly removed. All are fissured. Five contain gas and one contains fluid. (*B*) Roentgenogram made after two weeks of drying in room air. The fluid is gone, the fissures are wider and longer, and all contain gas.

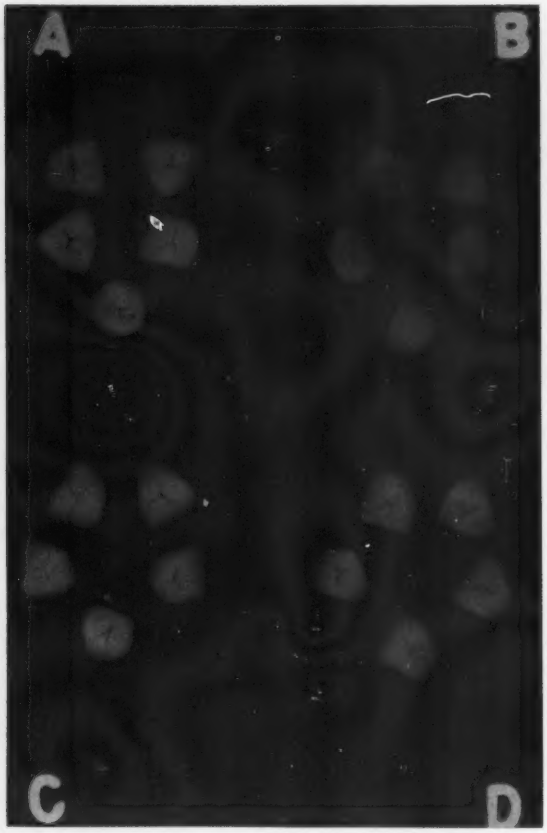

FIG. 5. *Solvent Action of Alcohol on Fissured Calculi.* Roentgenogram of a typical unit of twenty calculi from one patient. Appearance after two years' exposure to air (Group *A*), alcohol (Group *B*), normal saline (Group *C*) and formalin (Group *D*). These are 1.5 cm. calculi which have been dried. Fissures are present in the *A*, *C*, and *D* groups but they have been obliterated in the *B* group which was kept in 95 per cent alcohol.

the bottom of the flask. Roentgenograms made after the negative pressure interval show practically complete disappearance of the gas from the central void (Fig. 6*B*).

Presumably the gas passed through the grossly intact substance of the calculus in the direction of negative pressure and was replaced by water from the environment.*

* *Other Observations.* This same simple experiment was performed with other calculi containing gas-filled central fissures, and it was noted with interest that when the negative pressure was increased to 25 or 30 pounds, a number of calculi underwent complete fragmentation along the lines of the existing fissures. Evidently the sudden decrease of environmental pressure caused expansion of the entrapped gas which literally burst the calculi along the lines of least resistance. In each instance of fragmentation, the bubbles of gas could be seen to escape and the fragments settled to the bottom of the flask.

General Relation of Fissuring to the Formation and Nature of Gallstones. It is beyond the scope of this paper to go into the causes, composition, extensive classification schema and colloid-crystalloid internal structure of gallstones. It is widely accepted, however, that gallstones are formed in various ways. The pure cholesterol stones probably begin by "guttulate separation" in the presence of fat and form a true crystalloid concretion.[4] Mixed (common) gallstones, on the other hand, are colloid-crystalloid concretions containing impurities such as mucus, albumin, pigment, and calcium in varying proportions. Whether solidification is gradual or sudden and whether crystallization occurs from the inside outward or from the outside inward is not yet determined. The mechanisms of production of the concentric rings and the radial arrangement of the pulp are not fully understood, but must be considered as commonplace.

As previously mentioned,[2] the radial and dendritic splits associated with central fissure formation are seen in roentgenograms of aluminum spot welds.[5] The same process is manifested geologically in the cracking and buckling of the earth's surface. It is found on a small scale in hailstones, and also in various concretions formed by lower animals. Shrinkage cracks in steel or alloy ingots are of great importance in metallurgy.[3]

According to Schade,[4] with advancing age of concretions there is internal change in the coloids and crystalloids. The innermost structure shrinks and dendritic cracks extend peripherally, creating ruptures in the outer stratified layers. The radial fissures may extend to the surface creating cracks.

These purely physical phenomena of shrinkage and fissuring seem to us to explain fully the findings in biliary calculi. We do not believe that it is necessary to evoke anaerobic bacterial action, breakdown product disintegration, gaseous expansion, or other previously advanced theories to explain the common occurrence of fissures.

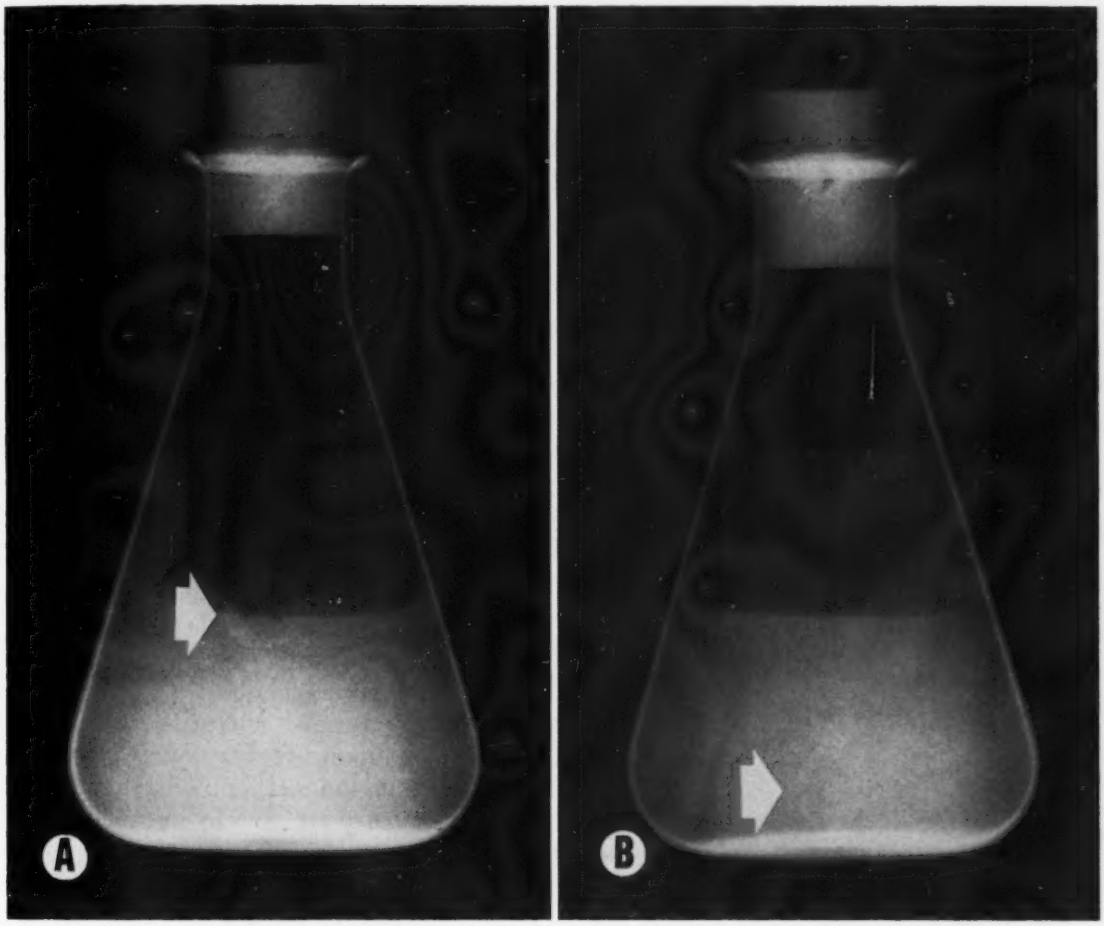

Fig. 6. *Diffusion of Gas Through Gallstone Immersed in Water and Mineral Oil.* Roentgenograms of nonopaque fissured calculus. In (*A*) the calculus (arrow) contains gas and floats buoyantly above the junction of the water with the mineral oil. (*B*) After the application of negative pressure, the gas has disappeared and the calculus has dropped to the bottom of the flask (arrow).

Why Do Some Calculi Contain Fluid When Others Contain Gas? From Table 1 it is apparent that 48 per cent of patients harbored fissured calculi filled with either fluid or gas. The gas-filled fissures in this series were usually small and centrally placed. They did not extend to the periphery. It is believed that the gas reached the central void by diffusion.

The fluid-filled fissures, on the other hand, were larger and extended to or almost to the periphery in most instances. It is our impression that these fissures actually extended to the periphery and that the fluid gained access to the central void through subvisible breaks in the surface continuity.

If one accepts the postulate that fissures form as the result of physical phenomena having to do with the shrinkage of crystals and colloids, then the central negative pressure void or "fault" will be filled with whatever substance can most easily gain access. If the stone is porous or actually cracked, the void will be filled with bile or bile fluids, as was the case in the calculi in Figure 7. If the stone is impervious to fluids, the gases dissolved in the surrounding fluids may gain access by diffusion. In summary, the fissures may be filled in any of the following ways:

(A) By inward diffusion of bile fluids if the calculus is porous.

(B) By an influx of fluid constituents of the

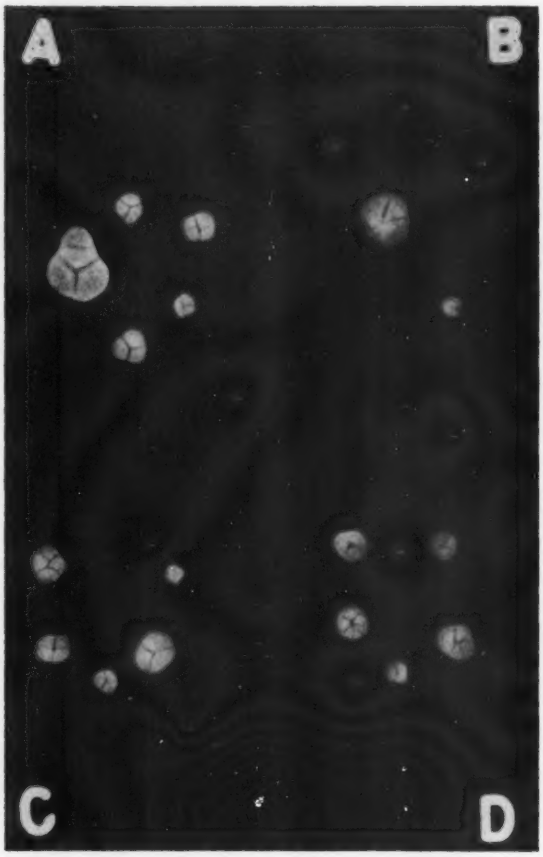

FIG. 7. *Extensive Peripheral Fissuring in Small Opaque Calculi.* Roentgenogram after drying. Groups *A*, *B*, *C*, and *D* are all fissured. The fissures extend to the external surfaces. On gross inspection these calculi resemble hot cross buns. In such concretions the fissures terminate in actual cracks.

bile if the fissures extend to and involve the periphery of the calculus.

(C) By inward diffusion of gases from the bile if the calculus is intact.

It is certainly conceivable that when a central void is formed, the gases may diffuse in first while the fluid comes later. As the shrinkage process continues, the fissures would be expected to extend nearer and nearer to the periphery, thus facilitating the entrance of fluid. Whether or not this is actually the sequence of events, probably it is the basic factor in spontaneous fragmentation. In the course of this series of experiments, we noted numerous instances of spontaneous fragmentation. It occurred only in fissured calculi.

Correlation of Gross Characteristics with Fissuring. Representative calculi of the 57 patients showing fissuring were cracked with a hammer and were observed with a hand lens. The gross characteristics[1] associated with fissuring are arranged below in order of frequency. Two or more of these characteristics were frequently noted in the same calculus.

Predominantly brown color	51	(90%)
Radial arrangement	40	(70%)
Concentric colored rings	35	(60%)
Glistening crystals	23	(40%)
Fissures recognized grossly	19	(33%)
Outside hard, smooth, brittle crust	16	(26%)
Granular or mud-like internal structure	7	(12%)

Pure pigment calculi and pure cholesterol calculi showed no fissures. It is noteworthy that on gross examination one sees colors, but cannot appreciate density variations or mineral deposition. Fissuring is poorly appreciated upon breaking open of calculi since trauma induces cracking along the fissures and they are thereby not recognized as such.

It appears from the above that fissuring is most likely to occur in brown calculi having a radial crystal arrangement and concentric colored rings. It is, however, seen with surprising frequency in calculi having other characteristics.

Correlation of Roentgenological Features with Fissuring. Upon roentgenological study of the calculi from the 100 patients referred to above, it soon became apparent that the roentgenograms correlated only roughly with the gross appearance. We could easily recognize layers of different densities but could neither appreciate the multicolored rings nor differentiate between nonopaque crystals of different character. Beautiful arrangements in many variations were observed. It was found that all calculi could be divided roentgenologically into five groups. Not all calculi from each patient presented the same appearance but when the calculi from each

patient were considered as a unit representative of the individual, the 100 patient-units were found to be distributed as follows:

	Patients
Nonopaque throughout	48
Dense periphery or crust	15
Opaque throughout	14
Alternating layers of opaque and nonopaque material	12
Dense center or nidus	11

It is of interest to divide the 356 fissured calculi into the same roentgenological groups in order to determine the characteristics most commonly associated with fissuring. Results are shown in Table II.

TABLE II

ROENTGENOLOGICAL CHARACTERISTICS OF 356 FISSURED BILIARY CALCULI

Nonopaque throughout	184	(51%)
Center or nidus opaque	62	(18%)
Alternating layers, opaque and nonopaque	47	(13%)
Opaque periphery	44	(12%)
Opaque throughout	18	(4%)

Comment: Fissured calculi are most commonly nonopaque or have a small opaque central nidus. Less frequently they show concentric layers of mineralization or are covered by a dense crust. Calculi which are dense throughout seldom fissure.

SUMMARY

1. Fissures in biliary calculi are very common. They were present in the fresh calculi of 48 patients in a series of 100 consecutive cholecystectomies. When the calculi were dried the patient incidence was 57 per cent. Most of the fissures contained fluid in the fresh state, but gas was seen in some, and in a few gallbladders fluid-filled and gas-filled fissures were found to coexist.

2. The identity of the material within fissures is influenced by the environment. Whether the contents are fluid or gaseous is probably dependent upon the size of the central void, the extent of the dendritic fissures and the porosity of the calculus and its shell.

3. When fissured calculi were dried in air there was loss of fluid from the fissures, shrinkage of the central substance, widening of the fissures and occasional spontaneous fragmentation.

4. Storage of calculi in physiological saline and 10 per cent formalin for one to two and one-half years exerted no appreciable effect on the incidence, character, or degree of fissuring. Ninety-five per cent alcohol caused dissolution of some calculi. In others, it decreased or obscured fissuring as a result of its solvent action.

5. Fissuring occurred most commonly in brown, radially constructed, nonopaque calculi and in those having a dense central nidus. It was uncommon in those calculi which were dense throughout or which were lacking in radial structure. It was not found in pure cholesterol or pure pigment calculi.

6. Fissuring is believed to be a natural physical phenomenon resulting from internal shrinkage of the colloid-crystalloid mass of the concretion. It is probably a manifestation of ageing and is influenced by composition, crystal arrangement and porosity.

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LOCALIZED ORGANIZING PNEUMONIA: ITS RESEMBLANCE TO CARCINOMA*

A REVIEW OF ITS CLINICAL, ROENTGENOGRAPHIC AND PATHOLOGIC FEATURES

By LAUREN V. ACKERMAN, M.D., GLADDEN V. ELLIOTT, M.D., *and* MARIO ALANIS, M.D.

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ORGANIZING pneumonia as a localized process has been seen by us as a surgical problem in 15 instances. This poorly defined entity has been mistaken clinically, roentgenographically, and usually at exploratory thoracotomy for carcinoma of the lung. As a surgical problem, with a few exceptions (Freedlander and Waddell), this process has been neglected. Recognition is imperative since conservative rather than radical surgical measures are indicated and in the reported cases a lobectomy rather than a pneumonectomy was possible in most instances. We are well aware that so-called "virus pneumonia," often represented by changing roentgenographic shadows, is frequently treated as a nonmalignant process only to find later that the roentgenographic signs were related to variable degrees of bronchial block by a carcinoma. For that reason, we are not advocating delay in the prompt exploration of localized pulmonary lesions of doubtful etiology. This lesion is relatively rare for during the time period in which these cases were collected more than ten times as many carcinomas of the lung were explored surgically.

CLINICAL EVALUATION

The clinical findings in this group of cases strongly suggest the diagnosis of bronchogenic carcinoma. Thirteen patients were male and 2 were females. Fourteen of the patients were over forty years of age and 11 were heavy somokers. The clinical symptoms were those of a chronic pulmonary disease. The most important single clinical finding in the background was a history in 10 instances suggesting the presence of lobar pneumonia. These patients had a rather typical onset with chills, fever and cough. There were signs of incomplete improvement following the administration of various antibiotics. These episodes at times were repeated. In 7 patients hemoptysis occurred and it was not infrequent for it to be repeated. Chronic cough, chest pain and shortness of breath were almost uniform. All these patients appeared chronically ill and weight loss was often a prominent feature. In 9 cases this amounted to a loss of 10 or more pounds. On the basis of this clinical history, the most logical diagnosis in this group of cases seemed to be bronchogenic carcinoma.

ROENTGENOLOGICAL EXAMINATION

The initial roentgenographic examinations were thought to be diagnostic of bronchogenic carcinoma in 10 out of the 15 cases reported. In 3 additional instances, bronchogenic carcinoma was considered as the second most likely diagnosis and could not be excluded. The 2 remaining cases were diagnosed as interlobar effusion and metastatic carcinoma.

The roentgenographic findings in the 13 cases in which bronchogenic carcinoma was considered may be divided into three types. The most common (9 out of 13) consisted of a segmental atelectasis with or without a hilar mass (Fig. 1). The right upper lobe was the most frequent site for this type of involvement. Two cases, representing the second type, revealed a hilar mass without atelectasis (Fig. 2), and finally, there were 2 cases with peripheral rounded or nodular

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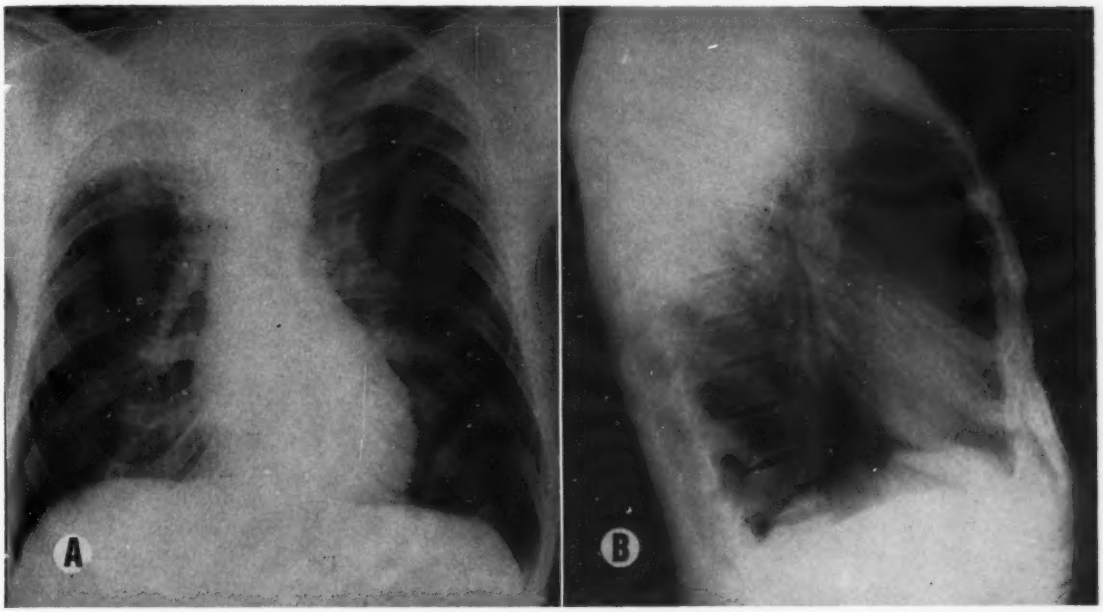

Fig. 1. Posteroanterior (*A*) and right lateral (*B*) roentgenograms of the chest of a forty-two year old white man clinically thought to have bronchogenic carcinoma. Homogeneous infiltration of the apical and subapical segments of the right upper lobe and the suggestion of a right paratracheal mass can be seen. The roentgenographic diagnosis was bronchogenic carcinoma. Exploratory thoracotomy with frozen section revealed organizing pneumonia.

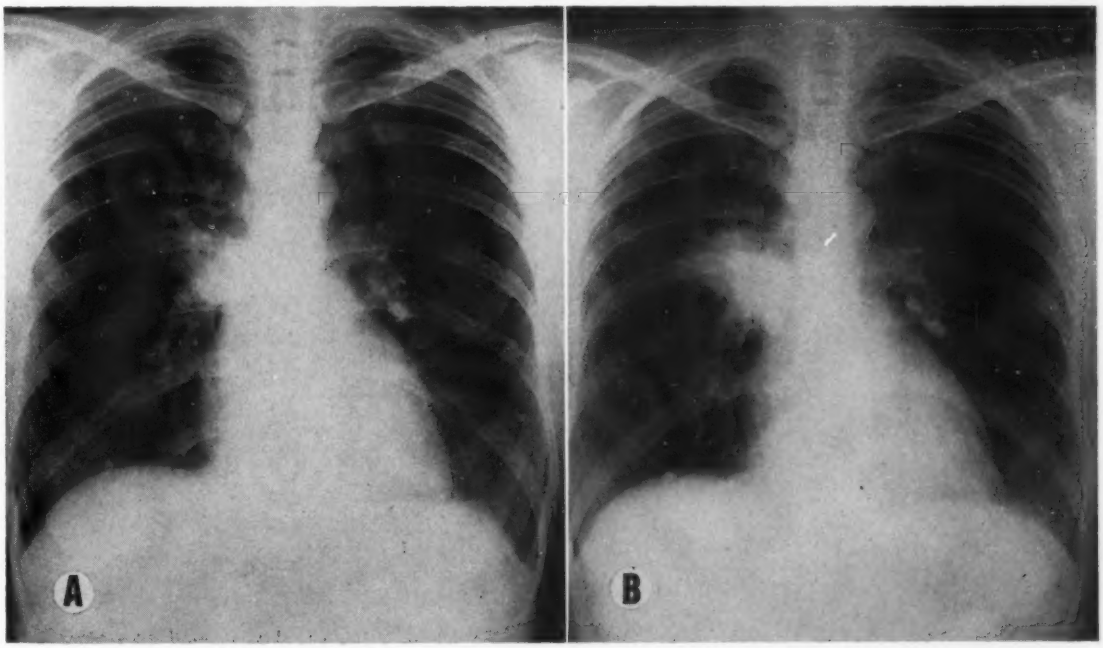

Fig. 2. Posteroanterior roentgenograms of the chest of a forty-four year old white woman on (*A*) January 26, 1948, and (*B*) September 13, 1951. A large right hilar mass was present on both examinations. Although originally thought to represent bronchogenic carcinoma, the relative lack of progression during the subsequent 3½ year interval militated against this diagnosis. Exploratory thoracotomy with frozen section proved this to represent organizing pneumonia.

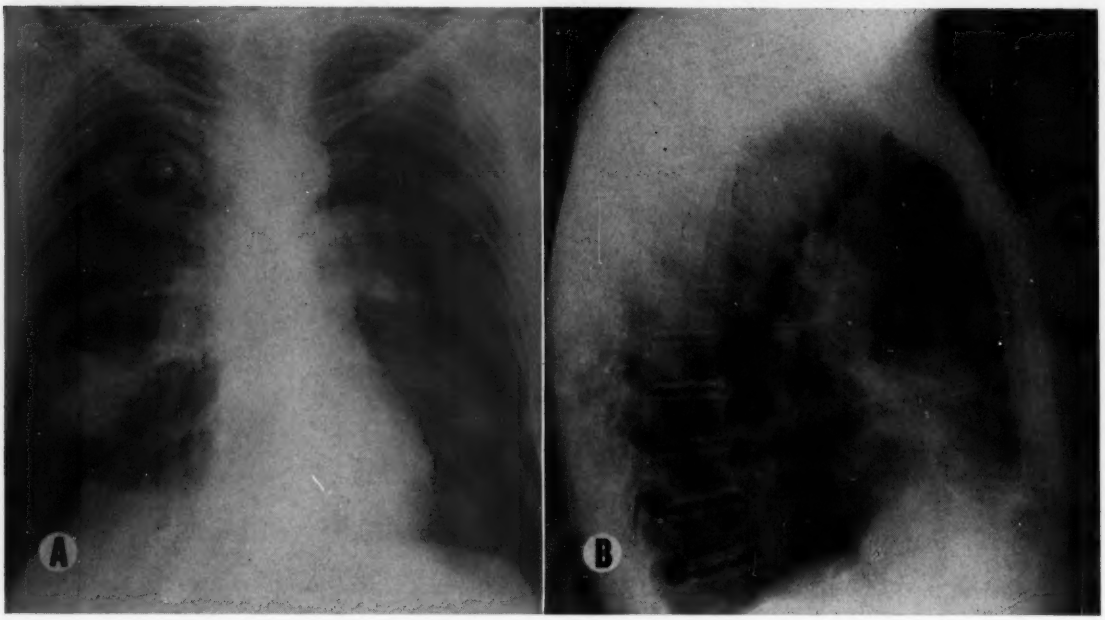

FIG. 3. Posteroanterior (*A*) and right lateral (*B*) roentgenograms of the chest of a seventy year old white woman. The rounded right middle lobe mass associated with enlargement of nodes at the inferior pole of the right hilus led to the roentgenographic diagnosis of bronchogenic carcinoma of the peripheral type. Pathological diagnosis was organizing pneumonia.

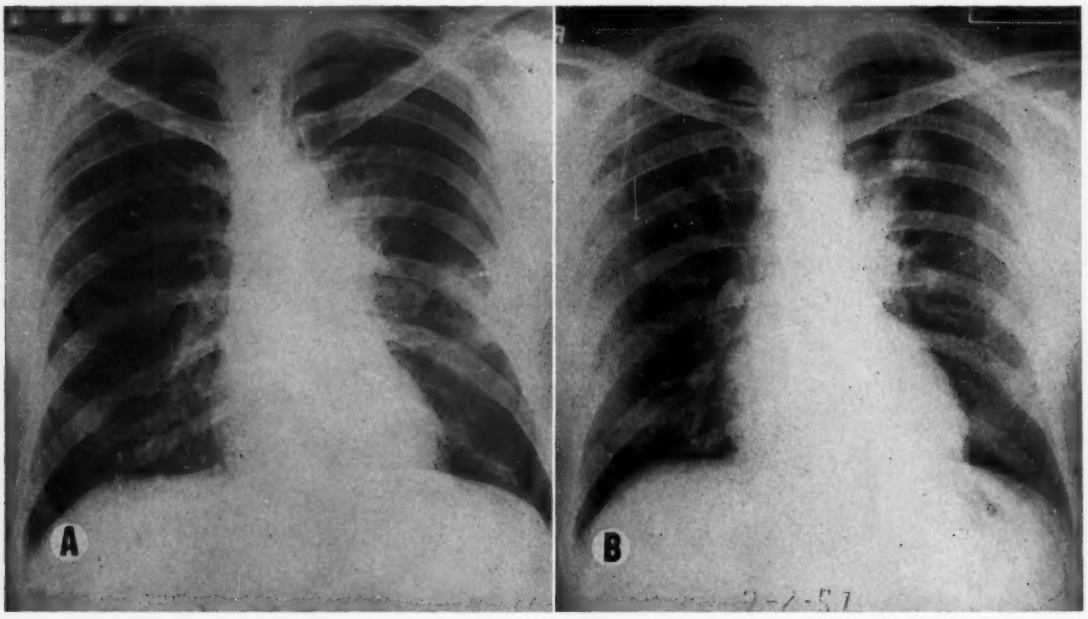

FIG. 4. Posteroanterior roentgenograms of the chest of a forty-one year old white male on (*A*) January 20, 1951, and (*B*) February 2, 1951. Migration of the pulmonary infiltration from the pectoral to the subapical segment of the left upper lobe with concomitant decrease in the size of the left hilar mass suggested inflammatory disease in spite of the clinical history. Exploratory thoracotomy with frozen section revealed organizing pneumonia.

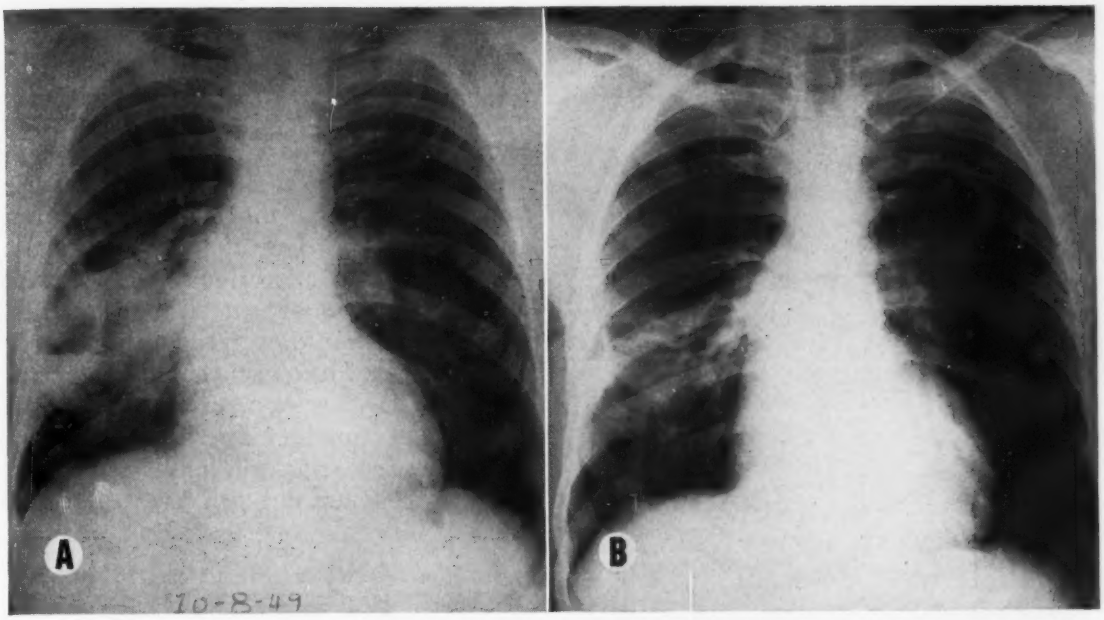

Fig. 5. Posteroanterior roentgenograms of the chest of a forty-seven year old white male on (*A*) October 8, 1949, and (*B*) October 19, 1949. Extension of the infiltrate to the pleural surface with formation of a loculated empyema and the rapid regression in eleven days favored an inflammatory process. The pathological diagnosis of organizing pneumonia verified this impression.

infiltrates (Fig. 3). These various findings follow closely the classical picture of bronchogenic carcinoma as described by Olds and Kirklin. Together with the usual clinical history, they seldom left much doubt as to the diagnosis.

It is important to point out, however, that additional roentgenological examinations in 4 of the cases originally classified as bronchogenic carcinoma led to the conclusion that the lesions were of inflammatory rather than neoplastic origins. In 2 of these cases a refusal of the patient to submit to surgery or the lapse of a sufficient time interval permitted sequential examinations which suggested that the processes were benign. In 1 of these instances (Fig. 2), the relative lack of progression of a hilar mass over a three year period was impressive. In the second case (Fig. 4), the migratory character of the pulmonary infiltrate indicated involvement of multiple segments and spoke against localized bronchial obstruction due to neoplasm.

Extension of infiltration to a pleural surface with formation of a loculated empyema in a third case (Fig. 5) was considered as evidence against bronchogenic carcinoma. The regression of this process in a period of eleven days was further evidence in this direction.

In only 3 cases were laminagrams or bronchograms obtained. In 1 of these instances (Fig. 6 and 7), the laminagrams clearly demonstrated a lack of bronchial occlusion which could have accounted for the atelectatic segment observed. Together with involvement of the pleural surface, this was felt to be strong evidence against carcinoma. In another case, laminagrams revealed calcification within a hilar mass. This suggested an inflammatory etiology. Bronchography was of no help in the 1 case in which it was performed. A more complete roentgenological examination of some of the other patients might have shown similar findings and thus have at least warned the surgeon that he might be dealing with a benign process.

The presence of a hilar mass in 10 of our

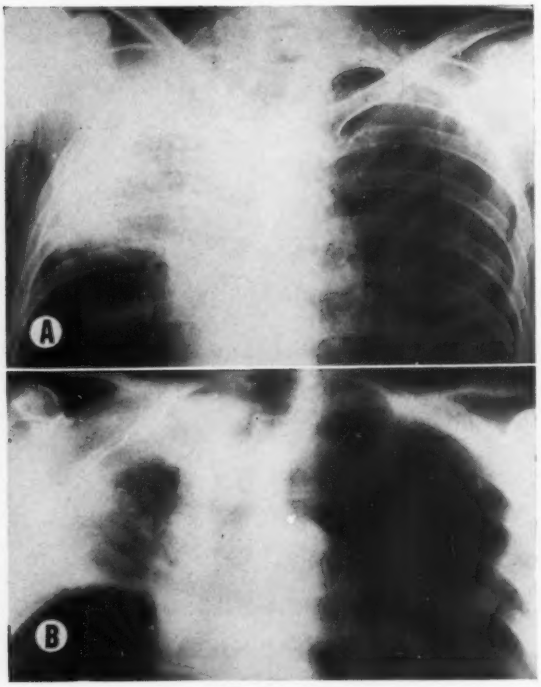

FIG. 6. (*A*) Posteroanterior roentgenogram of the chest of a seventy-eight year old white man revealing atelectasis of the right upper lobe and suggesting a right hilar mass. (*B*) Laminagram of the same patient revealing patent bronchi supplying the atelectatic segment. The lack of bronchial obstruction indicates an inflammatory atelectasis.

15 cases indicates that adenopathy is not a reliable diagnostic clue. Such adenopathy in the presence of an inflammatory lesion has been previously described (Freedlander and Wolpaw).

Those cases with peripheral rounded or nodular lesions and those with bronchial stenosis or compression on an inflammatory basis are difficult if not impossible to differentiate from carcinoma roentgenographically. Serial examinations do not seem justified when any given case may in reality represent carcinoma.

BRONCHOSCOPY

Bronchoscopy was done in all cases. In 1 instance a mass was seen which was thought to be carcinoma but subsequently proved to be merely an inflammatory mass. Biopsies revealed normal bronchus, chronic inflammation and/or squamous metaplasia of the bronchus.

EXFOLIATIVE CYTOLOGY

Exfoliative cytology was done in 14 cases. No tumor cells were identified in 13. Sputum smears from cases of organizing pneumonia have no characteristics which are specific for this disease, nor does the over-all picture of the slides suggest an inflammatory rather than a neoplastic process. In 1 instance, due to the presence of cells with prominent nuclei and nucleoli, a false positive interpretation of the smear was reported. However, this difficulty occurred as an exception rather than as the rule. In inflammatory diseases of the lung, malignant appearing cells may rarely occur; but such cells are not peculiar to any one of such inflammatory diseases (Jackson).

FIG. 7. Transected gross specimen of the right lung removed at exploratory thoracotomy. Patent bronchi extending into the consolidated right upper lobe are seen. Note thickening of pleura. Microscopic examination revealed only organizing pneumonia.

Taken as a group, the absence of tumor cells is significant for we find tumor cells in 80 per cent of our patients with resectable carcinomas. In an individual case, however, such a conclusion is not warranted, for that particular case may fall into the 20 per cent in which no tumor cells can be identified.

EXPLORATORY THORACOTOMY

These 15 cases were explored with the provisional diagnosis of carcinoma of the lung. The thoracic surgeon found the pleura thickened in all instances and in a few there was such extreme thickening of the pleura that fibrous tissue had extended into the soft tissues of the chest wall, thus making the dissection of the involved lung from the thoracic cage extremely difficult. We have recently seen a case, not reported in this series, in which the fixation of the process to the chest wall was so severe that the operation had to be abandoned.

FROZEN SECTION

The findings at operation, in most instances, were considered by the thoracic surgeon to represent carcinoma and for that reason frozen section was done in 11 instances and in another the resected lobe was inspected by the pathologist. A correct frozen section diagnosis of organizing pneumonia was made in all but 1 instance. In that instance an erroneous diagnosis of carcinoma was made by a new resident in pathology unfamiliar with this entity. In 2 instances the thoracic surgeon was so convinced that the process was carcinoma that more than one frozen section was done. With the pathological diagnosis of organizing pneumonia, the surgeon then performed a conservative procedure except in 3 instances where technical difficulties forced the removal of the entire lung. These difficulties included extensive adhesions and injuries to large blood vessels. After the lobe was removed it was again submitted to the pathologist and the bronchi were opened. This precaution is necessary, for occasionally organizing pneumonia may be secondary to a bronchogenic carcinoma. Only one error was made in the interpretation of the frozen section but the interpretation is often difficult. The pulmonary parenchyma is extensively altered by the process and appears extremely cellular. Further more, up to the time of the frozen section, the clinical diagnosis of carcinoma appeared certain. The frozen section may therefore come as a distinct surprise to the thoracic surgeon, and the pathologist must hold firm to what he sees microscopically.

GROSS PATHOLOGY

Organizing pneumonia has been described in great detail as an autopsy finding, and most of the German literature was well reviewed by Floyd. We can contribute little to their description.

The specimens we studied were rather similar. The process was confined to an upper lobe in 11 cases, to the middle lobe in 1 case, and to the lower lobe in 1 other. In 1 instance, both an upper and lower lobe were involved and in another the middle and lower lobes were both implicated. Fibrous thickening of the pleura and intralobular septa was severe and the lung felt firm. The bronchi were at times slightly dilated but in no instance was the major finding bronchiectasis. The bronchi were often diffusely reddened and at times superficially ulcerated in the small branches. In 4 instances the lung itself showed small areas of cavitation. These areas of cavitation were recent, had poorly defined walls, and did not have the gross appearance of a chronic abscess, and were therefore thought to represent areas of recent breakdown of pulmonary parenchyma. The color of the lesions varied from grayish-red to light yellow.

MICROSCOPIC APPEARANCE

The microscopic pattern of these cases was also rather similar. The changes in the bronchi were of particular interest for inflammatory lesions were present in both small and large bronchi. In the larger

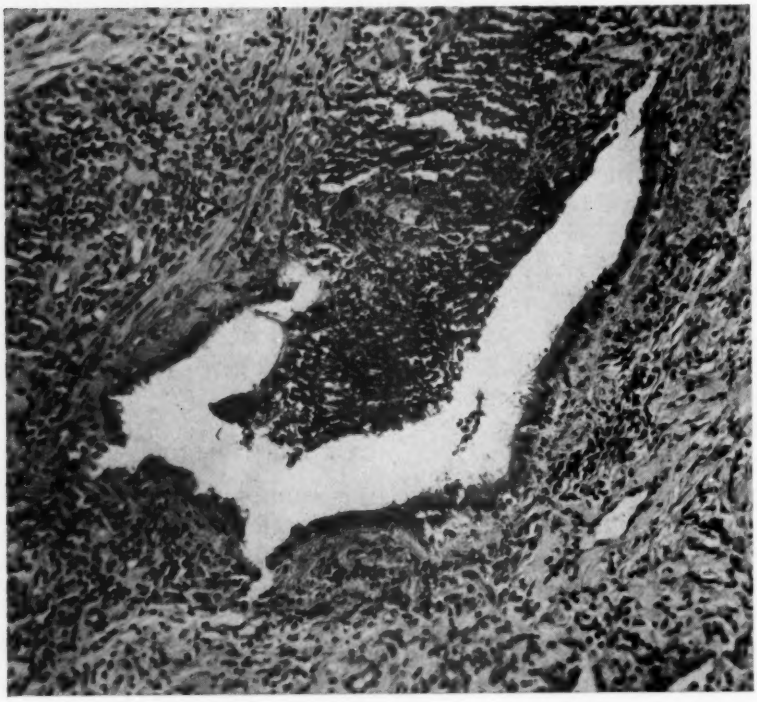

FIG. 8. Photomicrograph demonstrating ulceration and destruction of the wall of a small bronchus. An inflammatory plug of tissue is protruding into the lumen. Hemorrhage could occur from such areas. (×150)

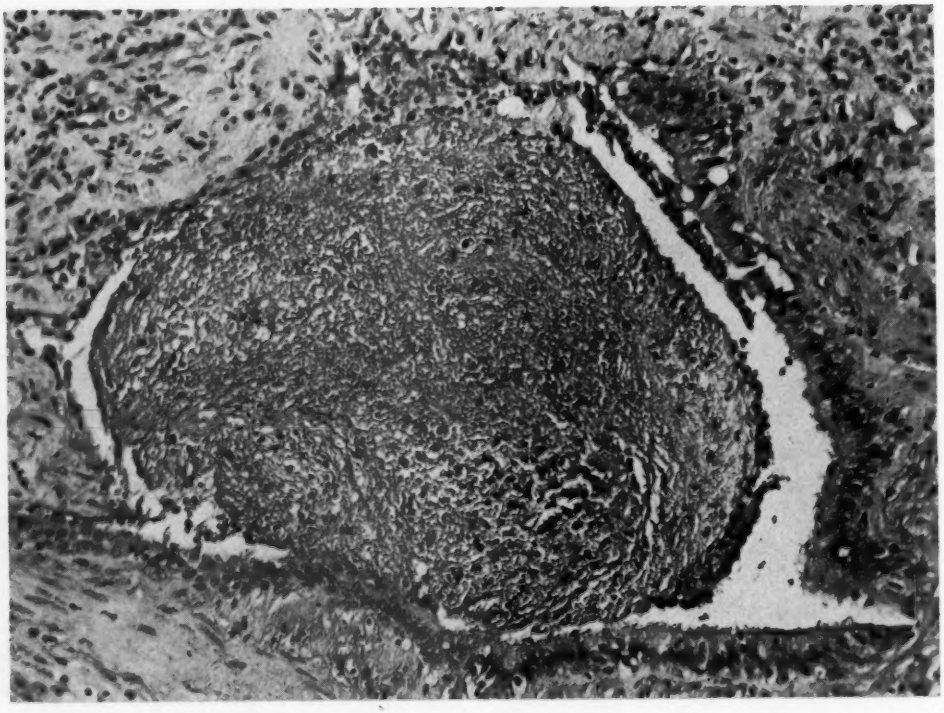

FIG. 9. Photomicrograph to demonstrate organization of exudate within a small bronchus. Such organization of exudate could cause small areas of atelectasis. (×175)

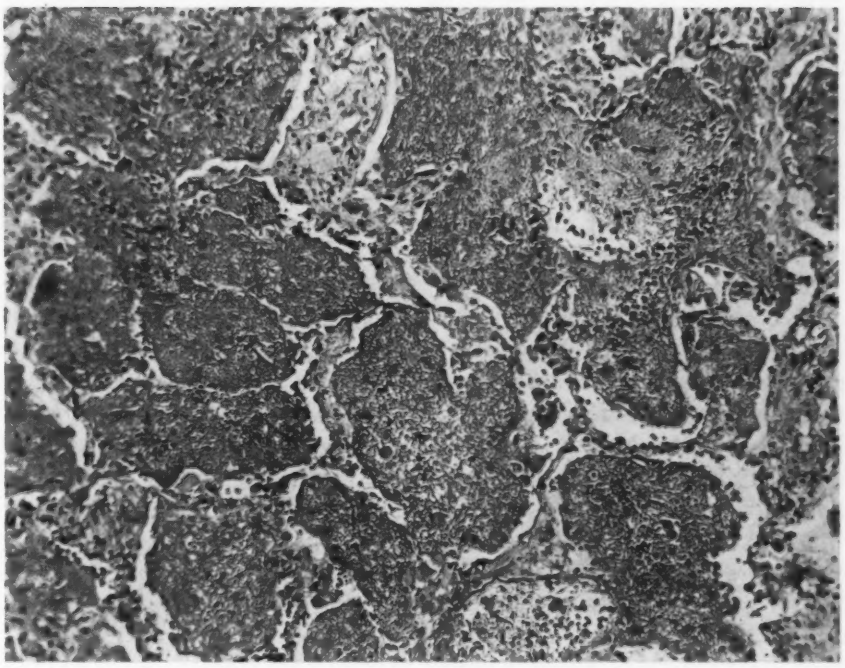

Fig. 10. Photomicrograph to demonstrate the organization of exudate within the lumen of alveoli. (×100)

bronchi there was at times partial destruction of the bronchial walls. Such destruction was common in the medium sized bronchi (Fig. 8). These destructive changes result in inflammatory masses protruding into the lumens. In a number of instances organization of the exudate within the bronchi occurred (Fig. 9). Intralobular and interstital fibrosis of minimal to marked degree were present. The connective tissue proliferation often extended into the pores of Cohn. There was a heavy inflammatory infiltrate present which was made up chiefly of mononuclears and plasma cells. In areas of necrosis, focal collections of polymorphonuclear cells were seen. In a few scattered instances single giant cells were observed. Macrophages filled with fat were present to a minimal degree and in no instances were there changes present which we would associate with exogenous aspirations of lipoid. There were no granulomatous lesions or fungi observed.

The pathogenesis of the process is obscure to us. Our bacteriologic studies, we feel, have been most inadequate. The clinical history that 10 patients had an early episode suggesting a possible pneumococcus pneumonia may be of some value. We may postulate that the pneumonia, instead of resolving, went on to organization with a slumbering persistent infection. Antibiotic therapy in many of our cases may have modified the appearance of the lesion. The available bacteriology together with the necrotizing changes in the bronchi suggest a mixed flora (Kershner and Adams). Bacteriologic stains in this group were non-rewarding. Streptococci are known to cause necrosis of bronchi (Harford). The infection may first have been caused by a pneumococcus and later complicated by the presence of other organisms.

DISCUSSION

These 15 cases of organizing pneumonia demonstrate that this entity is extremely difficult, if not impossible, to differentiate from bronchogenic carcinoma. The diagnosis might become obvious both clinically

and roentgenographically if sufficient time were allowed to elapse. This procedure, however, does not seem justifiable in the consideration of an individual case since undue delay may cause great harm if the lesion should prove to be malignant. It would appear, however, that more adequate roentgenological examinations, including the use of laminagraphy might indicate the correct diagnosis in a significant percentage of cases. The demonstration of patent bronchi, calcification within the mass, involvement of multiple segments, and extension to pleural surfaces are the roentgenological criteria favoring benignity. The roentgenographic suggestion that the process might be inflammatory may aid the pathologist and the thoracic surgeon at the time of surgery. In view of the pathology found in these cases, it seems unlikely that this process could ever fully resolve. The fibrous and chronic inflammation present results in chronic sepsis which accounts for the weight loss and the chronic illness which these patients have demonstrated. We have found, in contradiction to Freedlander and Wolpaw, that frozen section is diagnostic. Previous cases have been treated by immediate pneumonectomy, because the diagnosis of carcinoma appeared certain. With frozen section, lobectomy rather than pneumonectomy can be done. Such a procedure conserves pulmonary parenchyma and since many of the individuals in this group are over the age of forty this may reduce early and later respiratory insufficiency.

SUMMARY

1. Fifteen cases of localized organizing pneumonia have been reported.

2. Clinically and roentgenographically the diagnosis in almost all of the group was carcinoma of the lung. Possible criteria for a more accurate roentgenological diagnosis are outlined.

3. Frozen section is invariably diagnostic of organizing pneumonia, and lobectomy rather than pneumonectomy can be done.

4. The pathogenesis is obscure, but it may be related to previous unresolved pneumonia complicated later by other bacteriological agents.

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DISTANT METASTASIS FROM CARCINOMA OF THE ORAL CAVITY

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CARCINOMA of the oral cavity is considered to be a form of malignant disease which produces its mischief locally or, at most, regionally. Traditionally it has been taught that oral cancer does not spread below the level of the clavicle.[11,12,13,19]

Generally speaking, these concepts are true. Death usually results from the direct or indirect effects of the local lesion or the regional metastasis, not from remote or visceral metastasis.

In many cases, specific and nonspecific toxemia, dehydration and malnutrition combine to bring on inanition and death. In such cases, hypostatic bronchopneumonia and necrotizing pneumonia are often the immediate causes of death.

Less frequently, massive or repeated hemorrhage leads to death. Rarely death comes as a result of carotid body stimulation. Even more rarely encountered is the oral cancer patient who may elect to terminate his existence at a time of his choosing.

Disseminated or visceral metastasis, although not an important cause of oral cancer death, does occur and appears to be more frequently encountered in recent years.

Despite the fact that visceral metastasis is being discovered more frequently in oral malignancy, even so it is not a problem in the curative management of the disease.

As is well known, this is not the case when one considers the management of carcinoma of the breast, the stomach, the rectum and other important forms of malignancy. In these latter sites of cancer, visceral metastasis, often present even on admission, modifies fundamentally the treatment of the disease.

For example, in a series of 162 fatal cases of carcinoma of the breast, studied by Warren and Witham,[21] only 8 *did not* present distant metastasis. Of the 162 cases, 154 cases (95 per cent) presented distant metastasis in an average of five or more organs. Burch[3] states that the incidence of osseous metastasis in lethal cases of cancer of the breast approaches 100 per cent.

In lethal cases of cancer of the rectum, the incidence of hepatic metastasis has been reported to be 50 per cent.[13,23] Cancer of the stomach presents hepatic metastasis in 46 to 70 per cent of lethal cases.[20,23]

Another striking difference between oral cancer and malignancy in other important sites is the time of development of distant metastasis. In cancer of the rectum, the stomach, and the breast, visceral metastasis is frequently an early event in the course of the disease. Indeed, as previously mentioned, it is too often present when the patient is first seen. In cancer of the oral cavity, visceral metastasis is practically never an early event. We have never observed a case of oral malignancy with distant metastasis present at the time the patient first sought medical advice.

This paper presents an analysis of 752 cases of oral malignancy proved by biopsy. The purpose is to determine the probable incidence of distant metastasis. We propose to answer these questions—What chance does a patient with oral malignancy have of developing distant metastasis? Of what clinical importance is distant metastasis in oral malignancy?

Most of the reported instances of distant metastasis have been reported on the basis of autopsy experience. Willis,[23] in reporting on 64 necropsies of patients with carcinoma

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about the head and neck (including 25 cases involving the pharynx, larynx and tonsil), states that 25 cases, or 39 per cent, had visceral metastasis. In another communication[22] he states that he found visceral metastasis in 8 of 20 autopsies (40 per cent) in patients with carcinoma of the tongue, while in carcinoma of the pharynx and tonsils, he found visceral metastasis in 11 of 27 autopsies (40 per cent).

Braund and Martin,[2] using autopsy material only, found distant metastasis in 23.2 per cent (66 cases) of 284 cases. However, of these cases, 160 involved the tonsil, nose and paranasal sinuses, pharynx, larynx and esophagus. At this point, it should be interjected and emphasized that distant metastasis is more common in carcinoma of the laryngo-pharynx than in carcinoma of the oral cavity proper.[14,22,23]

Reporting the incidence of distant metastasis on a basis of autopsy experience only tends to lead to the conclusion that the incidence of distant metastasis is higher than is actually the case. The reasons for this are clear. It must be pointed out that the majority of oral cancer patients who die never come to autopsy. Many patients suffering in the final stages of oral cancer die outside the hospital. Many patients who die in the hospital do not come to autopsy because efforts to obtain permission often fail in this type of case because the cause of death seems so obvious to all. A case of oral malignancy with distant metastasis presents an added challenge to any resident in his desire to obtain permission for an autopsy. All this undoubtedly tends to magnify the apparent incidence of distant metastasis when studied on a basis of postmortem results.

It would seem more rational to report cases of distant metastasis on a basis of total experience, rather than on autopsy experience. By so doing, a clearer conception of the small part that distant metastasis plays in the problem of oral malignancy can be obtained.

In Table 1, it can be seen that of 200 patients known to have died from cancer of the oral cavity from 1930 to 1943, only 2 per cent presented evidences of distant metastasis.

Of 121 patients known to have died from cancer in the period from 1943 to 1951, 10.7 per cent presented evidences of distant metastasis. Martin,[15] in reporting on cancer of the tongue, found distant metas-

TABLE I

SITES OF PRIMARY LESIONS WITH DISTANT METASTASIS

	1930–1943				1943–1951			
	Total No. Treated	Known Dead from Cancer	No. with Distant Metastasis	Per Cent with Distant Metastasis of Known Dead from Cancer	Total No. Treated	Known Dead from Cancer	No. with Distant Metastasis	Per Cent with Distant Metastasis of Known Dead from Cancer
Carcinoma of lower lip	127	40	0	0	99	19	0	0
Carcinoma of tongue	109	69	1	1.5	110	47	5	10.6
Carcinoma of floor of mouth	33	20	0	0	52	21	6	28.6
Carcinoma of buccal surface	48	26	0	0	37	11	1	9.0
Carcinoma of lower gingiva	61	35	2	6.0	41	18	0	0
Carcinoma of upper gingiva	22	10	1	10.0	13	5	1	20.0
TOTAL	400	200	4	2.0	352	121	13	10.7

tasis in 12 of 556 cases treated. Reporting on other categories,[16,17,18] he found distant metastasis in approximately 1 per cent of 103 cases of cancer of the floor of the mouth; 2 per cent of 99 cases of cancer of the buccal surface; and five per cent of 113 cases of cancer of the gingiva.

Braund and Martin[2] doubt the accuracy of clinical judgment in determining the presence of distant metastasis. It cannot be argued that in an occasional case not subjected to autopsy a patient may die with *unrecognized* distant visceral metastasis. It must be emphasized, however, that visceral metastasis *can be* accurately diagnosed in a high percentage of cases if sound clinical judgment, re-enforced with a full knowledge of the behavior pattern of oral malignancy, is exercised. In our series, roentgen evidences of metastasis in lung or bone, or both, were present in approximately 75 per cent of cases. Clinical evidence of hepatic involvement, of cerebral involvement and of involvement of the skin and muscle in distant sites increases the likelihood of accurate clinical diagnosis in these cases to more than 80 per cent. In our series, when the clinical evidences of distant metastasis were checked with the autopsy findings, this was found to be true.

With the advent in our institution of precision intraoral irradiation,[4,7,8] and newer techniques in the treatment of cervical metastasis,[5,6,10] it has been possible to sterilize a great many more local lesions together with their cervical metastases. For example, in carcinoma of the floor of the mouth, we have been able to bring about primary control of the local lesion in 55 per cent of cases in the past eight years, as compared with 18 per cent in the preceding thirteen years. In carcinoma of the tongue, we have been able primarily to control the local lesion in 52 per cent of cases in the past eight years, as compared with 23 per cent in the previous thirteen years. In carcinoma of the buccal surface, we have been able to bring about primary control of the local lesion in 70 per cent of cases in the past eight years, as compared with 35 per cent in the preceding thirteen years. By using preoperative irradiation to hold in check the cervical metastasis, while the local lesion is being brought under control, we have been able to perform neck dissection on many patients who would have deen denied this procedure in the past, thus controlling more cases of cervical metastasis.[10] Through the development of improved irradiation techniques, the management of advanced cervical metastasis has carried with it considerably more hope for long term palliation. Much higher roentgen radiation doses delivered with far greater safety to more rigidly controlled portals has contributed importantly to the lengthening of life of the patient suffering from oral cancer. The extension of surgical horizons likewise has contributed. The improved methods of interstitial radon or radium element needle implantation, in various combinations with roentgen irradiation and surgery and the use of supervoltage radiations,* all have contributed to this improved picture.

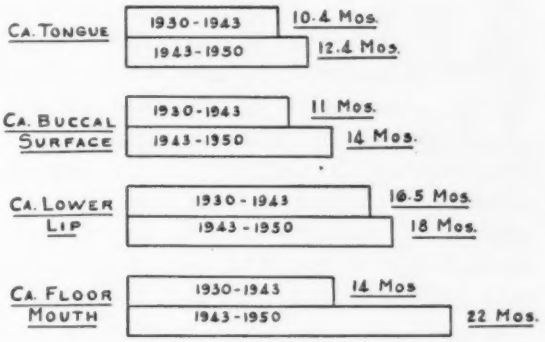

Chart 1. Duration of life in treated fatal cases.

This increased span of life after therapy in treated fatal cases is illustrated in Chart 1. In cases of carcinoma of the lower lip, seen from 1930 to 1943,† the average survival after therapy in treated fatal cases was

* Supervoltage irradiation delivered at a potential of approximately 1.75 mev. (1,750,000 volts).

† The periods 1930 to 1943 and 1943 to 1951 were selected inasmuch as radical changes in treatment methods were introduced in 1943 by the senior author (S.G.C.).

16.5 months. In a comparable series of cases seen from 1943 to 1951, the average survival in treated fatal cases was eighteen months. Carcinoma of the floor of the mouth showed the greatest increase in survival time after therapy. In the former period (1930 to 1943), fatal cases lived an average of fourteen months after treatment, while in the later period (1943 to 1951), the average duration of life after treatment was twenty-two months, an average increase of eight months.

Carcinoma of the tongue showed an increased survival of from 10.4 to 12.4 months and carcinoma of the buccal surface showed an increase from 11 months to 14 months.

Braund and Martin[2] found no relation between the histopathologic grade of the lesion and frequency of distant metastasis. Interestingly, they likewise found no relation between the length of time that the lesion had been present before treatment and frequency of distant metastasis. This would suggest that perhaps an increased life span following treatment, in fatal cases, should have no bearing on the incidence of distant metastasis. However, coincident with an increase in survival time in these patients, instances of distant metastasis are being observed with greater frequency.

Even though we have been able to control many more local lesions, a considerable number of these patients still die from uncontrolled cervical metastasis. In other less common instances, when both the primary lesion and the cervical metastasis have been controlled, visceral metastasis still causes the death of the patient.

In 4 of 17 cases of distant metastasis studied, both the primary lesion and cervical metastasis were controlled. In 7 cases the primary lesion was controlled but the cervical metastasis was not. In the remaining 6 cases neither the local lesion nor the cervical metastasis was controlled.

It is apparent that in most of the cases of oral carcinoma which developed visceral metastasis, either the primary lesion or the cervical metastasis or both were not controlled (13 of 17 cases). If the primary oral lesion and regional cervical metastasis are controlled, the patient will practically never develop visceral metastasis (4 cases in 321 lethal cases of oral malignancy). This is in sharp contrast to the course of malignancy originating in other sites. It is a well known fact that visceral metastasis develops in a discouragingly high percentage of cases of cancer of the stomach, rectum, and breast, even though the local disease and its regional spread are controlled.

In Table 1, the instances of distant metastasis observed are listed in relation to the number of cases of carcinoma in each site treated during the periods 1930 to 1943 and 1943 to 1951. Not a single case of distant metastasis developed from carcinoma of the lower lip, in the cases studied. In carcinoma of the tongue, 1 case of distant metastasis was observed during the earlier period; while in the more recent period, 5 cases have been observed. In carcinoma of the floor of the mouth, not a single case of distant metastasis was observed in the earlier period, while in the more recent period, 6 cases of distant metastasis have been seen (see Table 1). There has likewise been an increase in distant metastasis in carcinoma of the buccal surface. In the earlier period no cases were noted as compared with 1 case in the 1943 to 1951 period.

It is of interest to note that the increased incidence has been the greatest in carcinoma of the tongue and floor of the mouth. Carcinoma of the floor of the mouth which showed the greatest increase in survival time of treated fatal cases (14 months to 22 months), likewise showed the greatest increase in the incidence of distant metastasis (see Chart 1). In the former period (1930 to 1943) not a single case developed distant metastasis, while in the latter period (1943 to 1951) 28.6 per cent of treated fatal cases developed visceral metastasis. This would suggest that with an increase in life span of treated fatal cases, the likelihood of the development of distant metastasis also increases.

TABLE II

SITES OF DISTANT METASTASIS

Cases with Distant Metastasis	Lungs	Bone	Liver	Brain	Skin	Muscle	Peritoneum	Heart	Kidneys	Small Intestine
Carcinoma of lower lip No cases	0	0	0	0	0	0	0	0	0	0
Carcinoma of tongue 6 cases	5	2	2	1	0	0	0	0	0	0
Carcinoma of floor of mouth 6 cases	5	2	2	0	1	0	1	0	0	0
Carcinoma of buccal surface 1 case	1	1	1	1	1	1	0	1	1	1
Carcinoma of lower gingiva 2 cases	2	1	0	0	0	0	0	0	0	0
Carcinoma of upper gingiva 2 cases	1	1	1	0	0	0	0	0	0	0
TOTAL	14	7	6	2	2	1	1	1	1	1

During the period from 1930 to 1943, 200 treated cases were known to have died of cancer despite treatment. These cases were distributed over six sites of origin (see Table 1). Of these 200 cases, 2 per cent showed distant metastasis. During the period from 1943 to 1951, 121 cases were known to have died of cancer despite treatment. These cases were distributed over the same six sites of origin as above (see Table 1). Of these 121 cases, 10.7 per cent showed metastasis, a fivefold increase.

The lung is probably the organ most frequently involved with distant metastasis. Willis[22,23] found visceral metastasis, in order of frequency, in the following organs: lung, 19 cases; liver, 14 cases; kidneys, 8 cases; bones, 5 cases; heart, 4 cases; adrenal, 4 cases; thyroid, 3 cases; spleen, pancreas, and muscles, 2 cases each; and stomach, intestine, brain, urinary bladder and gallbladder, 1 case each.

The sites of distant metastasis in our series are tabulated in Table II. The lung was involved in the greatest number of cases (14) (Fig. 4). The vertebrae were involved in 7 instances and the liver in 6 cases. The brain and remote skin areas each were involved in 2 instances. Muscle, peritoneum, heart, kidney, and small intestine were each involved in 1 instance. In the 1 case that involved the peritoneum, the lesion was located over the appendix and was found at exploratory laparotomy when the patient developed signs and symptoms suggestive of acute appendicitis.

The following case presented the most widespread visceral metastasis of the 17 cases studied. Since it is the only case that presented a metastatic lesion in the heart, it is deemed worthy of detailed report. It should be emphasized that this case developed visceral metastasis despite the fact that the primary oral lesion and radically operated neck metastasis remained under complete control.

CASE REPORT

E. B. (C-10620), a white male aged forty-five, was first seen in the head and neck clinic of the American Oncologic Hospital on February 10, 1950, with an obviously malignant lesion of the

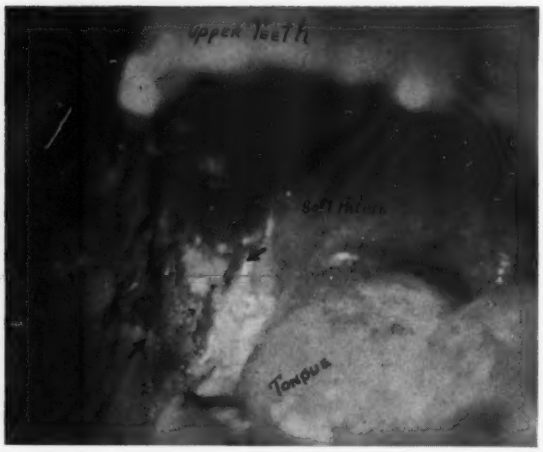

FIG. 1. Carcinoma of the right buccal surface. The extent of the lesion is indicated by the arrows. The lesion was 2.5 cm. in diameter and extended from the lower gingivobuccal sulcus to the occlusal line (see case report).

right posterior buccal surface (Fig. 1). The lesion was of six months' known duration. One month prior to admission, the patient consulted his dentist because of supposed irritation of the buccal surface by a tooth.

After being referred to his family doctor, he was in turn referred to the head and neck service of this clinic. On admission, there was an indurated lesion involving the right posterior buccal surface and extending from the lower gingivobuccal sulcus to the occlusal line. It measured at least 2.5 cm. in diameter.

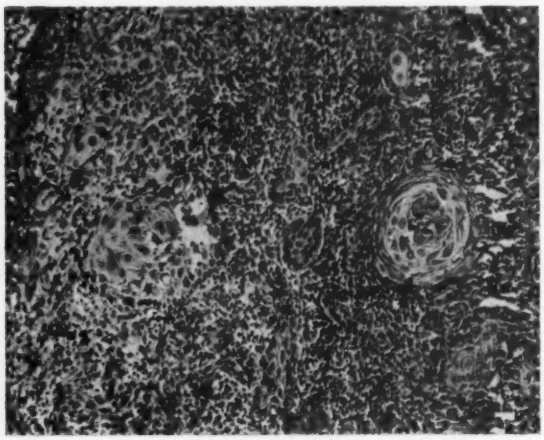

FIG. 2. Photomicrograph of the primary lesion of the right buccal surface. Note the nests of infiltrating cornifying squamous cells (arrows). A tendency toward pearl formation is evident. The lesion was classified as Grade 2.

A biopsy of the lesion was performed and the patient's teeth were removed in preparation for radiation therapy. The histopathological report was epidermoid carcinoma, squamous cell type, Grade 2 (Fig. 2). Peroral roentgen therapy was started using a specially prepared and shaped lead cone.[7] Between February 20, 1950, and March 24, 1950 a total dose of 7,500 r (in air) was delivered intraorally. The following factors were used: 200 kv. (peak), 25 ma., 42 cm. target skin distance 0.5 mm. Cu plus 1.0 mm. Al filtration, half-value layer 0.9 mm. Cu. This dose was supplemented by 4,200 r (in air) delivered through a right cheek portal measuring 5.1 cm.

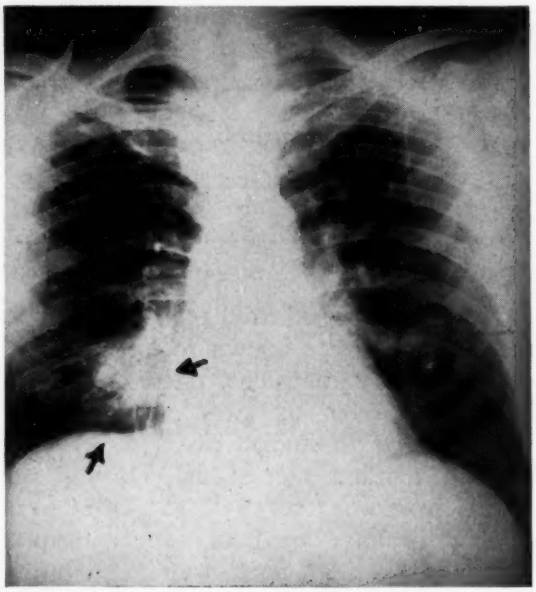

FIG. 3. Roentgenogram of the chest. Note the large metastatic lesion in the right lower lung field as indicated by arrows (see case report).

in diameter, using essentially the same factors. This treatment was delivered through a filter of 1.0 mm. Cu plus 1.0 mm. Al. The half-value layer was 1.2 mm. Cu. The total tumor dose to the right buccal surface was approximately 10,300 r. A brisk epidermitis and heavy ulcerative mucositis developed. The reaction healed within six weeks.

On June 2, 1950 the right postvascular lymph node was palpable. A clinical diagnosis of metastasis was made. Under local anesthesia, using cervical nerve block, a right radical neck dissection was performed on June 14, 1950. The histopathological report showed metastatic carcinoma in four submaxillary lymph nodes.

The remaining numerous lymph nodes studied showed no metastasis. The jugular vein was not invaded.* The patient was discharged from the hospital two weeks later after an uneventful postoperative course.

In September, 1950, a nodule 1 cm. in diameter was noted in the right mid-pectoral region. A clinical diagnosis of possible metastasis was made. A biopsy was performed and the histopathological report was epidermoid carcinoma, squamous cell type. To treat the lesion a dose of 7,000 r (in air) was delivered, between the period of September 18, 1950, and October 17, 1950. The following factors were used: 140 kv. (peak), 15 ma., 35 cm. target skin distance 0.5 mm. Cu plus 1.0 mm. Al filtration.

Fig. 4. Roentgenogram of the chest of a patient suffering from carcinoma of the floor of the mouth. The primary lesion was controlled by means of peroral irradiation. Multiple foci of cervical metastasis developed bilaterally during the course of therapy to the primary lesion. Pulmonary metastasis then developed shortly after treatment to the cervical metastasis was started. A course of nitrogen mustard therapy was of no benefit. Four months later the patient developed hepatic metastasis and died.

* All but one of the patients studied by Willis[22,23] that presented visceral metastasis had invasion of the jugular vein. Braund and Martin[3] likewise comment on jugular vein invasion. In only 1 of the 17 cases studied in this series was invasion of the jugular vein found.

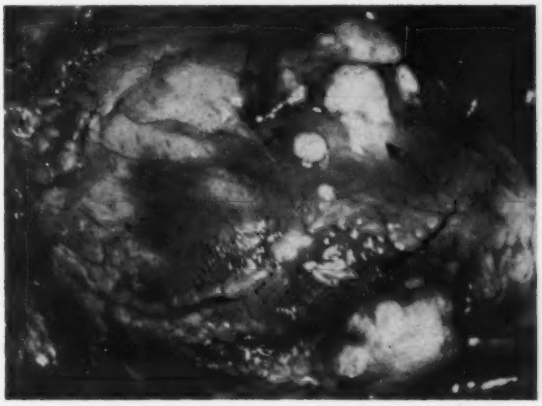

Fig. 5. Photograph of the heart in the case reported. Note numerous metastatic nodules involving the ventricular walls.

On October 30, 1950, a nodule 1.5 cm. in diameter was noted in the left temporal area, undoubtedly another metastatic nodule. At about this same time, the patient complained of vague pain in the lumbar area which became increasingly severe. Biopsy of the temporal lesion revealed epidermoid carcinoma, squamous cell type. A roentgen bone survey and intravenous urogram at this time were normal. Roentgen study of the chest, however, revealed a metastatic lesion in the right lower lung field (previous films had been normal) (Fig. 3).

On October 30, 1950, he was admitted to the hospital. His temperature chart showed a daily rise to 101°F. The patient had weakened considerably. He was given a course of nitrogen mustard. Four doses of nitrogen mustard, methyl-*bis*(β chloroethyl)amine, were administered. This resulted in a decline of the white blood cell count from 12,000 per cu. mm. at the start of the nitrogen mustard therapy to 1,400 per cu. mm. twelve days later. The white count

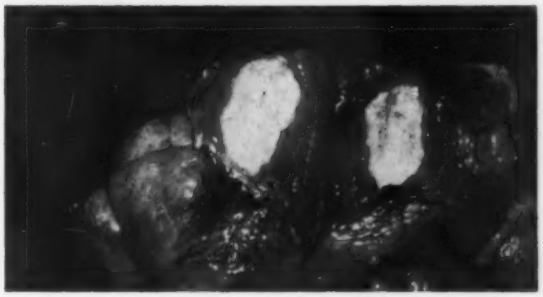

Fig. 6. Photograph of the heart in the case reported. Cross section of one of the larger metastatic lesions.

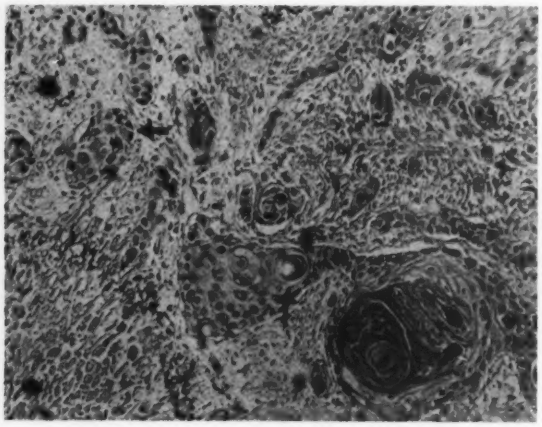

FIG. 7. Photomicrograph showing metastatic squamous cell carcinoma involving the heart. Arrows point to some of the nests of carcinoma cells infiltrating the striated cardiac muscle fibers. Note the large epithelial pearl.

was restored to normal by two blood transfusions. Nonetheless, the patient's condition gradually deteriorated and cerebral symptoms developed with loss of vision and nystagmus.

The patient died on November 10, 1950. *Autopsy revealed no evidence of local recurrence in the oral cavity or the neck.* In the left temporal area a subcutaneous metastatic nodule fixed to the periosteum which measured 1.5 cm. in diameter was noted. Involving the left deltoid muscle, was another metastatic lesion 5 cm. in diameter. Several ribs were involved with metastatic nodules 1 to 2 cm. in diameter. The treated area of metastasis over the right pectoral region showed no gross residual disease.

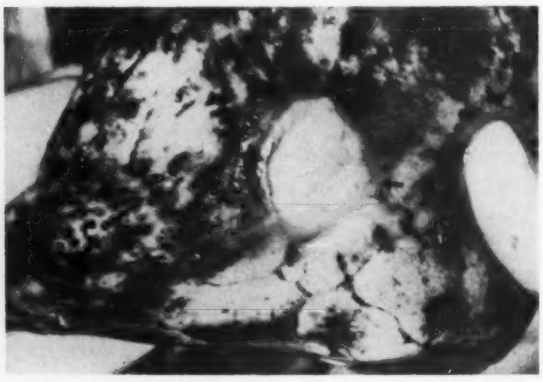

FIG. 8. Photograph of the lung in the case discussed. Note the large metastatic lesion involving the right lung.

The lungs were studded with white hard nodules varying up to 1.5 cm. in diameter (Fig. 8). The heart contained several metastatic lesions in the right and left ventricular walls, measuring 1 to 3.5 cm. in diameter (Fig. 5 and 6). The spleen was enlarged but contained no metastasis. The liver was enlarged and contained fifteen to twenty metastatic lesions varying from 2.4 to 3.0 cm. in diameter. Each kidney contained five or six metastatic lesions. The brain presented several metastatic lesions. The distal ileum presented a subserosal metastatic nodule.

Histopathologically the lesions were all epidermoid carcinoma, squamous cell type (Fig. 7).

Final pathologic diagnoses: (1) squamous cell carcinoma right buccal surface (controlled); (2) metastasis to right cervical region (controlled); (3) visceral metastasis involving the lungs, bones, liver, brain, skin, muscles, heart, kidneys, and small intestine.

SUMMARY

Distant metastasis from oral carcinoma is infrequent. In a study of 752 cases of oral carcinoma, 321 patients were known to have died from cancer. Of this number, 17 died of visceral metastasis, an incidence of 5.3 per cent.

In the period from 1930 to 1943, 2 per cent of 200 treated fatal cases studied showed distant metastasis. In the period 1943 to 1951, 10.7 per cent of 121 treated fatal cases studied showed distant metastasis.

With an increasing ability to control the local lesion together with its cervical metastasis, we have noted an increase in the life span in treated fatal cases. Coincident with an increased survival time in these patients, distant metastasis is being observed with greater frequency.

In addition, it is not unlikely that an increased interest in the advanced cancer patient is today uncovering cases of distant metastasis formerly missed.

In our experience the organs most frequently involved with distant metastasis from oral carcinoma are the lungs and

bones. Malignancy situated posterior to the anterior pillar of the tonsil is more prone to produce distant metastasis than malignancy which originated in the oral cavity.

We feel that it would be more rational to report cases of distant metastasis on the basis of total experience rather than on autopsy experience. By so doing a clear conception of the small part that distant metastasis plays in the problem of oral malignancy can be obtained.

Visceral metastasis can be accurately diagnosed in a high percentage of cases, if sound clinical judgment re-enforced with a full knowledge of the behavior pattern of oral malignancy is exercised. An accurate clinical diagnosis of distant metastasis was made in 80 per cent of the cases studied.

A case of epidermoid carcinoma, squamous cell type, Grade 2 involving the buccal surface is presented to demonstrate distant metastasis from oral malignancy. Numerous organs of the body, including the heart, were involved with metastatic foci.

Despite the recently noted increase in the incidence of visceral metastasis associated with oral malignancy, distant metastasis is still far from being the menace it is in other forms of cancer—for example, cancer of the breast with its high rate of metastasis to bone and lung or cancer of the rectum and cancer of the stomach with their high rates of metastasis to the liver, etc. Nonetheless, survey roentgenograms of the lungs and bones should be routine prior to contemplated radical surgery for advanced primary and secondary disease.

Generally speaking and admitting of exceptions, the problem of cure in oral malignancy is control of the local disease and its regional metastatic spread. If this admittedly difficult task is accomplished, the patient nearly always is cured. In other serious forms of cancer, *viz.*, cancer of the breast, rectum, stomach, etc., even though the primary and regional disease are permanently controlled, the patient in a discouragingly high percentage of cases is later doomed by the development of distant metastatic disease. This rarely happens in oral malignancy.

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HODGKIN'S DISEASE*

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HODGKIN'S disease presents a syndrome protean in manifestation in a relatively short-lived but usually fatal course. More often than not, it is first recognized by the involvement of peripheral lymph nodes, although it may arise anywhere in the auxiliary lymphoid system. It may be localized, but almost inevitably becomes generalized. It is a disease of contrasts, at once benign and malignant.

To date, there are no real clues as to its etiology. Perhaps the French label, "maladie de frontier," is more apt; that is, an illness on the borderline of inflammation and neoplasm.

Sternberg[28] in 1898 felt that Hodgkin's disease represented lymphatic tuberculosis. Dorothy Reed[22] in 1902 made a classical contribution to the study of this disease with her lucid description of its histopathology and concluded that tuberculosis had no direct bearing on the development of this entity. Ewing[6] stated that tuberculosis follows Hodgkin's disease like a shadow. It has been our experience that tuberculosis is not as commonly associated with Hodgkin's disease as the literature would indicate. Suffice it to say that tuberculosis appears in combination with Hodgkin's disease more often than with any other disease and that it may simulate Hodgkin's disease, especially when pulmonary changes are present.

The intracerebral inoculation of rabbits with extracts of granulomatous lesions producing an encephalitis was first described by Gordon.[9] It is a nonspecific response. Normal marrow or pus produces the same response. The reaction seems more related to the eosinophilia than to any specific property of the Hodgkin's emulsion.

Recently, Karnofsky and his associates[13] investigated the viruses and their relationship to lymphogranuloma. This group found that implantation of Hodgkin's disease tissue on the chorioallantoic membrane of a fertilized chick embryo produced an edematous reaction. This was observed only with inoculation of a Hodgkin's extract. This effect, however, could not be transmitted.

Currently, with the interest in the hormonal theory of disease, many speculated as to the relationship of the anterior pituitary and the adrenal cortex to Hodgkin's disease. Nothing definitive has as yet come from these studies. More than one hundred and twenty-five years after its first description, Hodgkin's disease remains etiologically an enigma.

Symmers,[30] as early as 1924, offered the concept that Hodgkin's disease is an affection of the hematopoietic system. Robb-Smith[23] places Hodgkin's disease under the reticuloses, a heterogenous group believed to arise from the reticuloendothelial system and the lymphoid tissues.

Gall and Mallory[7] follow a cytological classification which appeals to us. They point out that Hodgkin's lymphoma is essentially polycellular, that the only elements which can be regarded as pathognomonic and whose presence is universally admitted as essential for diagnosis of the lesion consist of stem cells which tend to develop large multilobed or multinucleated forms. These are not found in any inflammatory process of established etiology. Hence, they are unconvinced of the utility of Hodgkin's granuloma. Jackson and Parker's[12] division into paragranuloma and granuloma is, in our opinion, a distinction without a difference.

The diagnosis of Hodgkin's disease based on anything else but histopatho-

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logical evidence is always questionable. It has been our custom to insist on a biopsy prior to treatment. Obviously, a mediastinal mass without associated nodes cannot be biopsied. In such a case the so-called therapeutic test of irradiation may be given with proper appreciation of its limitations.

Hodgkin's disease afflicts males more commonly than females and is found more often in the third decade of life. It may first appear limited to a few cervical lymph nodes. If not halted there by appropriate treatment, it sooner or later becomes generalized. The appearance of more than one group of peripheral lymph nodes heralds the silent involvement of the abdominal lymph nodes and viscera. Jackson and Parker,[12] on the basis of 63 cases examined postmortem, declare that the primary site of the disease was in the abdominal lymph nodes or viscera in 46 cases. They do not reveal how they reach this startling conclusion but, as Scott[25] says, if it is accepted, it should alter all our views in treatment.

Certain regions are anatomically susceptible to extension of this disease. Thus, the neck, axilla and mediastinum may be considered a unit; while the groin, abdominal and retroperitoneal areas can be thought of as constituting another unit. Mediastinal Hodgkin's disease without demonstrable peripheral lymph nodes is not uncommon. Scott says that 50 per cent of neck lesions in his series had associated mediastinal disease.

The spleen is involved in 75 per cent of cases, while the liver is less commonly damaged. The gastrointestinal tract, particularly the stomach and small intestine, is frequently the site of disease. One of our patients (J.D.) entered with abdominal distention. At operation an obstructing lesion in the terminal ileum was found. The pathologist's report was Hodgkin's granuloma.

Reports on the incidence of osseous involvement vary widely. Skeleton surveys and postmortem examinations are rarely complete. Golding,[8] Stout,[29] and Steiner[27] report 10, 18 and 28 per cent of bone lesions.

Dickson and Smitham,[5] in a study of 100 cases found 27 instances of pulmonary disease. Verse, quoted by the above authors, feels that one-third of all cases of Hodgkin's disease have pulmonary invasion.

Lesions may occur within the kidneys, adrenals, retroperitoneal and mesenteric systems. Direct involvement of the central nervous system is rare.

There is one type of this disease frequently overlooked. We are familiar with the patient who has lost weight, has no appetite, is pale, febrile or afebrile, and complains of pruritus. There are no grossly palpable lymph nodes; yet, careful roentgen studies may reveal pulmonary, intra-abdominal or osseous disease. This form has often been labeled atypical.

Until recent years arsenic, surgery and irradiation, singly or in combination, have been the treatments of choice in Hodgkin's disease. Surgery would only seem indicated when the disease is localized and when a radical dissection is performed. Most authors prefer postoperative irradiation when localized lymph nodes are radically removed. Holmes and Schulz[11] state that it makes very little difference whether localized lesions are treated with surgery or irradiation. If the latter is used, they recommend a tumor dose of 3,000 roentgens. Portmann[21] feels that the results with irradiation are superior to the combined form. One patient of our present series (T.C.) is now living and well twelve years after "a partial axillary dissection for Hodgkin's granuloma," followed by a single intensive course of irradiation.

The patient with a localized lesion is the exception rather than the rule. Hence, low, intermedite and high voltage irradiation has been employed for obvious lymph node groups, while teleroentgen therapy, total body irradiation or so-called roentgen baths have been used for generalized disease. There is no unanimity as to field size or the number of portals to be employed. Intensive treatment is reserved for the localized lesion. Otherwise, fractionation with a protracted treatment time is ad-

vised. We suggest that a combination of voltage and filtration be used which yields a diminished surface dose with the maximum penetration desired.

We have not employed so-called prophylactic irradiation as employed by Peters.[20]

In Minot and Isaacs'[18] group of 401 cases of lymphoblastoma, the average duration of life ws 2.76 years; 1 of their cases lived 17¾ years. They say the type of case that naturally lasts long is the one with the slow rate of progress early, spontaneous remissions, and apparently with the initial lesions developing in parts of the body readily accessible for therapy.

Yet we are convinced that some patients undergoing treatment are able to live beyond the anticipated survival time when properly managed. Survival rates for this disease as published by various authors are not comparable, since some take as the base line the first recognizable symptom, others the onset of initial therapy. Bethell *et al.*,[1] in a review of 119 cases, found that 19.3 per cent were living at five years. Boden,[3] reporting on 112 cases of Hodgkin's disease, observed that 26 per cent were living at five years. Craver,[4] reviewing 471 cases, found that 23.6 per cent were living at five years, while of 265 cases seen in an earlier series only 17.7 per cent were living. He attributes this improvement to a greater appreciation of regional involvement, greater accuracy of roentgen treatment, more intensive management of localized lesions and the availability of ancillary modes of treatment. Kasabach and McAlpin,[15] in analyzing 251 cases, where 65 were actually followed, found that about 40 per cent were alive at five years, provided the treatment was adequate.

Since the last review by one of us[19] in 1940, we have seen 170 patients in clinic or office referred for radiation therapy of Hodgkin's disease. There were 27, or about 15 per cent, who had some other disease. Twelve were carcinoma, 5 tuberculosis, 6 were elsewhere in the lymphoma group, 3 were sarcoid and 1 undiagnosed.

The remainder, 143 cases, were proved Hodgkin's disease either by biopsy or postmortem. There were 15 of the group which were not treated because they fell into the acute fulminating stage of the disease or were terminal.

Of the remaining 128 cases, only 1 was reported in a prior series and is included here because of his readmission to the hospital, the one by the way who lived the longest.

There were three times as many males as females. In the series here reported, the average age was forty-six years, the oldest seventy-six and the youngest five and one-half years. The average delay before treatment was 7.5 months, the shortest elapsed time 2.5 weeks, and the longest 2 years. Survivals are figured from the first day of radiation therapy.

There were 31 patients with the disease initially localized to one or more groups of peripheral nodes. There are 11 of this group, or 35.4 per cent, surviving without clinical disease beyond five years. One patient is living ten years and 1 at twelve years. Still another, who was living and well twenty years after a radical neck dissection and postoperative irradiation, was admitted in his twenty-first postoperative year with mediastinal disease and died three years later. In addition to the 11 surviving without clinical disease, there are 3 more patients of this group who are living but with clinical disease at five years, giving a combined five year survival rate of 45 per cent.

Of 97 patients who had generalized disease on admission, 59 were dead within one year, an additional 29, or 88, were dead before three years. There were, however, 9 cases surviving at five years, 1 without demonstrable disease, something less than 10 per cent.

Clinically, the cervical and abdominal lymph nodes were most frequently first recognized as the source of demonstrable disease in our series. Of the patients having involved lymph nodes of the neck, 24 per cent also had intrathoracic disease dis-

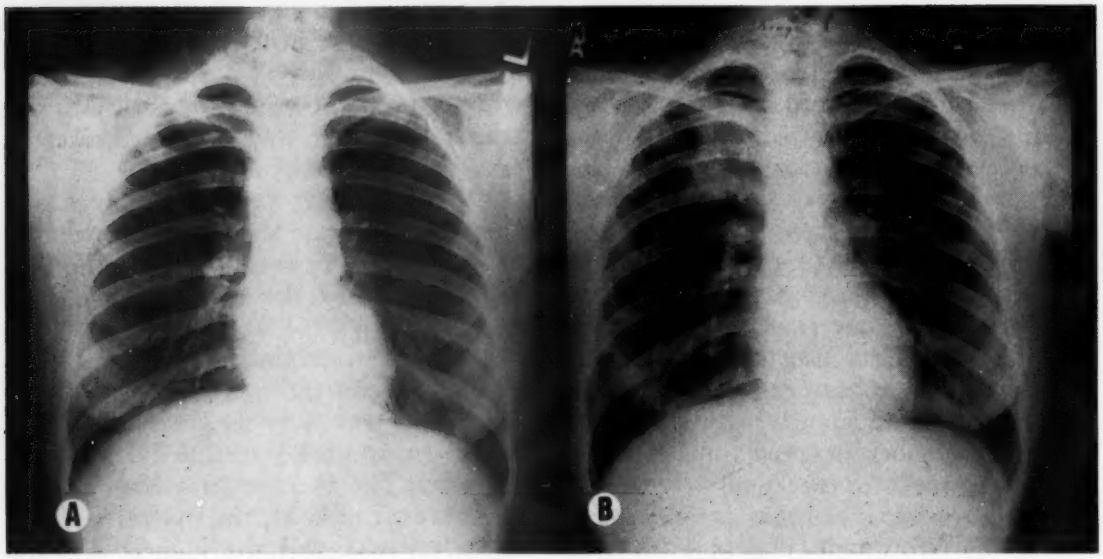

FIG. 1. (*A*) Clinical diagnosis of pulmonary tuberculosis. (*B*) Same patient after diagnosis of Hodgkin's disease was established.

covered by routine roentgenograms. There were actual pulmonary lesions demonstrated in 5 patients, 1 of whom (M.K.) was thought to have tuberculosis (Fig. 1). It was not until biopsy of a later appearing neck lymph node was done that the diagnosis of Hodgkin's disease was established. Sputum and gastric washings on this patient gave no definite information.

There were 3 patients with pulmonary tuberculosis who also had Hodgkin's disease. In 1 of the series a diagnosis of pulmonary tuberculosis with cavitation was made, which later proved to be Hodgkin's disease without tuberculosis (Fig. 2). Robbins[24] says that cavitation occurred in pulmonary Hodgkin's disease in about 5 per cent of his series.

The response to irradiation of intrapulmonary lesions is in many instances quite satisfactory (Fig. 3). However, the danger of pulmonary fibrosis as a possi-

FIG. 2. (*A*) and (*B*) Diagnosed clinically as pulmonary tuberculosis which proved to be Hodgkin's disease without tuberculosis.

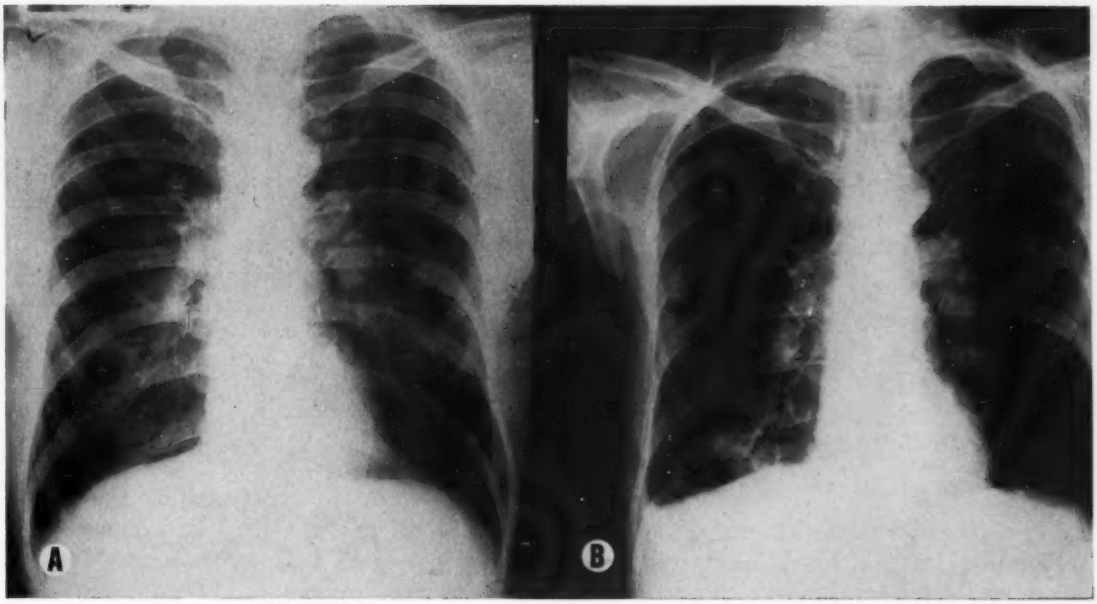

Fig. 3. Intrapulmonary Hodgkin's disease before (*A*) and after (*B*) radiation therapy.

ble sequel must be considered. To differentiate in the roentgenogram between irradiation fibrosis and lymphatic spread of tumor is not always a simple problem. Figure 4 illustrates the type of change considered as fibrotic metaplasia. Figure 5 probably represents actual pulmonary involvement by Hodgkin's disease as this patient received treatment only once to the mediastinum.

Bone lesions also respond favorably. When they occur, they are osteoblastic or osteolytic. Figure 6 illustrates an osteolytic

Fig. 4. Hodgkin's disease with pulmonary fibrosis. This patient has had no radiation to the lungs.

Fig. 5. Positive lymph node biopsy with pulmonary involvement by Hodgkin's disease.

Fig. 6. Osteolytic lesion of Hodgkin's disease involving right pubis.

lesion of the right inferior pubic ramus in a woman (J.T.) who also had intrapulmonary and mediastinal disease. Figure 7*A* illustrates an expanding destructive lesion of the proximal fibula; Figure 7*B* is the same patient one year after irradiation of this lesion. Figure 8*A* is a primarily osteolytic lesion with some new bone formation in the left inferior pubic ramus of the same patient; Figure 8*B* is the same lesion some two years after treatment.

Six of our series received one or more courses of nitrogen mustard. One had localized disease which responded to roentgen therapy. Without consultation this patient was given nitrogen mustard and died within two years. Five other patients had generalized disease and all had previous irradiation. One improved and remained well for eight months. One failed to respond to the first course, but became objectively better following a second course given two months after the first. Three patients failed to respond. Nausea and vomiting occurred in all patients.

What then is the position of the mustard derivatives in the treatment of Hodgkin's disease? Since the World War I discovery that victims of mustard gas developed a leukopenia, further study revealed that these chemical compounds acted as cytotoxins towards the lymphoid series. In a manner of speaking, the response is not unlike that observed following exposure to ionizing radiation. For these reasons the therapeutic value of the mustards was investigated.

Bichel,[2] in an excellent review, explains

Fig. 7. (*A*) Hodgkin's disease of fibula. (*B*) One year after irradiation.

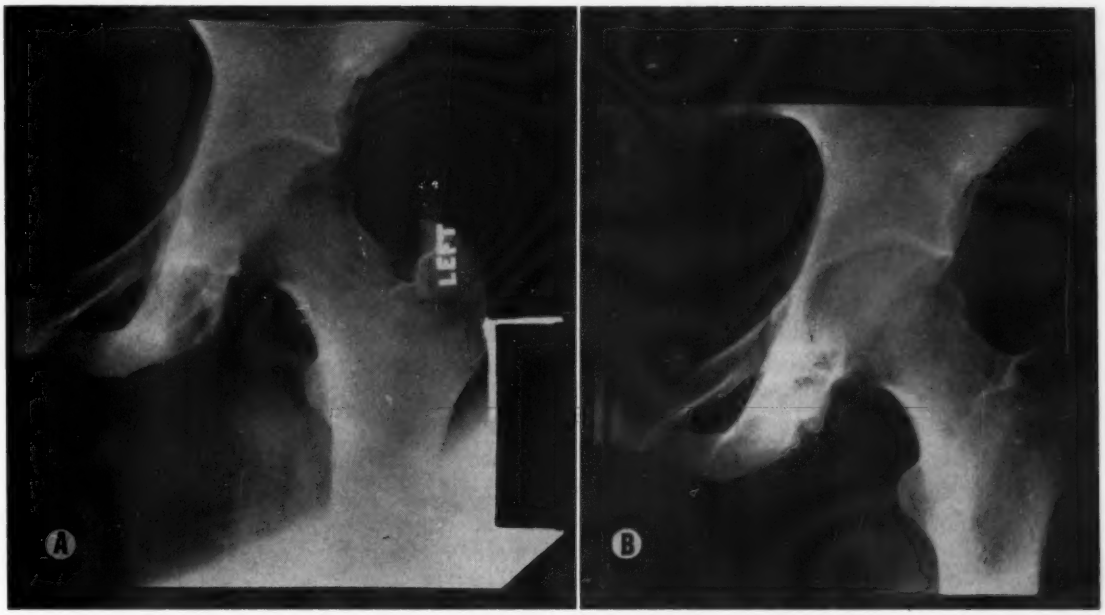

Fig. 8. (*A*) Osteolytic lesion of Hodgkin's disease of left pubis.
(*B*) Same lesion two years after treatment.

that all chemotherapeutic agents are cytotoxins and that there is no substance known capable of differential destruction of malignant tissue. This, then, is the key to the understanding of these chemical agents. This does not mean they cannot be used but militates against their promiscuous employment.

Cellular response will be proportionately greater in tissues where mitotic activity is greatest, thus the reason for its use in the treatment of malignant lymphomas. In addition, it must be emphasized that malignant growths are not histopathologically uniform in their maturity patterns and will not react to these agents in a similar manner.

Spitz[26] studied the histopathology of tissues exposed to nitrogen mustard therapy. Of normal tisssue, the bone marrow and testes were most easily damaged. Hypoplasia, granulocytopenia, hemorrhage and edema were observed. In the majority of cases examined there was irreversible testicular atrophy.

She examined histopathologically the tissues of 57 patients, 12 of whom had Hodgkin's disease, 16 lymphosarcoma, 9 lymphatic leukemia, 7 myelogenous leukemia, and 13 with other malignancies. The cases of lymphosarcoma presented the most striking alterations, which is in contrast to the clinical response observed. The changes in Hodgkin's entity were less striking. They consisted of swelling of the cytoplasm with a lipid material and ballooning and loss of the chromatin within the nuclei. Little, if any, change was observed in the other members of the group studied. The same author was unable to detect the alimentary changes seen in animals. Yet there must be some metaplasia, how else explain the gastrointestinal side effects which almost universally occur.

The clinical merit of the mustards has been studied by many. As a rule, only cases refractory to irradiation and those with the generalized form of the disease were treated. The *bis* form of nitrogen mustard, methyl-*bis* (B-chloroethyl) amine, is preferred, the *tris* form having been found too toxic. The side effects are manifested principally in the gastrointestinal tract, bone marrow and locally

at the site of injection. Nausea, vomiting and anorexia occur within two to eight hours and may last for as long as eighteen hours. The symptoms vary in duration and severity. Nearly all patients will experience them. Their occurrence and intensity diminish with successive courses.

The hematopoietic embarrassment is usually full blown within three weeks following the first injection. A lymphopenia is the initial response, followed by granulocytopenia and thrombocytopenia. An anemia rarely occurs. Because of this leukopenia, these drugs are to be used with caution in the presence of severe infections. All patients on such treatment should have complete blood counts and smears regularly.

Objectively, there may be improvement in the well being of the patient, a reduction of the over-all size of the lymph nodes, reduction of fever and occasionally relief of bone pain and pruritus. Remissions are usually short lived. The clinical palliation becomes less effective with successive doses. Some authors report shrinking of mediastinal disease.

Kieler[16] reported 36 cases, of which 22 had Hodgkin's disease. Improvement lasting from two to six months was noted in 15 cases, while 7 showed no response. Tucker and Kay[31] reported on 24 patients with the generalized form of the disease. Ten patients responded to a single course of nitrogen mustard, 5 required two courses and 1 required a third course. There were 8 patients who failed to respond. Remissions were variable and unpredictable. This author observed 2 patients who, radiation fast prior to mustard, became sensitive after a course with the drug. Wintrobe and Huguley[32] studied 102 cases treated with nitrogen mustard. Patients with Hodgkin's disease had the best results. Remissions lasted many months. There were 32 patients with Hodgkin's disease. Of these, 13 were living fifteen months from the beginning of treatment. Of the entire series, 17 cases had a good response, 5 had a fair response, and 10 showed no improvement.

Another agent with nitrogen mustard-like activity capable of oral or intravenous use is available. Karnofsky and co-workers[14] have described the clinical trial of triethylene melamine. In a study of 13 patients receiving this drug intravenously, no immediate or delayed local reactions were observed. Nausea and vomiting occur, but less frequently. Bone marrow depression occurs and is more pronounced than with the mustards. If this is too severe, hemorrhage and fever appear, terminating in death of the patient in two weeks.

Of the 13 cases studied, 6 showed an improvement lasting on the average five weeks. One of these patients with no previous treatment was in remission for twelve months. Seven cases did not benefit. Oral administration was attempted. Twenty-five patients received the drug by this route. The therapeutic and toxic effects were similar to the intravenous route. About one-third of the group benefited for a few months.

Hansen and Bichel[10] treated 9 patients with triethylene melamine. All were generalized cases. All had previous treatment. Four cases improved somewhat. They warn against the small therapeutic range of this drug. They observed a very insidious onset of bone marrow depression with a delayed appearance and requiring many months before clearing.

Leucutia,[17] reporting the annual meeting of the Swiss Society of Radiology at Lugano in May, 1951, given over chiefly to a symposium on Hodgkin's and allied diseases, states that Prof. Perussia's experience with nitrogen mustard at the Institute of Milan proved rather disappointing, that he was convinced that radiation therapy will continue to occupy the most important place and Prof. René Gilbert, Director of the Institute of Radiology of the University of Geneva, reached the over-all conclusion that radiation therapy constitutes the treatment of choice.

We believe the mustards and triethylene melamine may be useful adjuvants in the treatment of generalized Hodgkin's and so-

called radiation-fast disease. We are not so reactionary as to believe that chemotherapy may not have opened up an important approach to the treatment of the lymphoma group. We deprecate, however, their use routinely by internists and hematologists in early or late disease, without regard to the natural history of the disease and the known benefit of irradiation. A close collaboration between internist, surgeon and radiation therapist is essential. Until further evidence is presented, we feel that irradiation remains the cornerstone of therapeusis in Hodgkin's disease.

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DISCUSSION

DR. WILLIAM HARRIS, New York, New York. Dr. O'Brien has given us an excellent summary of the various approaches to the treatment of Hodgkin's disease.

I would like to call to your attention several situations which call for treatment other than radiotherapy. These are in patients who have compression syndromes such as a superior vena cava syndrome or compression of the spinal cord with or beginning paraplegia. In these cases the use of roentgen radiation does not bring about a rapid enough response to employ this agent. It has been found that the use of nitrogen mustard where compression exists will give a more rapid and often lifesaving result. This may, later on, after the bone marrow has returned to normal, be followed by a course of radiotherapy.

I should also like to mention the use of cortisone in patients with Hodgkin's disease who go on to hemolytic anemia. We have found the use of this drug extremely valuable in these conditions.

VOL. 71, NO. 6

THE EFFECT OF FLUORINE-FREE FOOD ON DENTAL AND PERIODONTAL STRUCTURES AS REVEALED BY ROENTGEN STUDIES

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THE value of optimum concentrations of fluorine in drinking water in the prevention of dental caries has been established. Probably more than one hundred and forty American communities already fluorinate their drinking water supplies.[1] It is remarkable, however, that so few data are available concerning the *direct* relationship of fluorine *in foodstuffs* to dental caries.[2] The study of this relationship in the rat is the purpose of this report.

In attempts to extract halogens from natural foodstuffs, two difficulties arise: (1) complete extraction is impossible, and (2) when extraction is done, other essential nutrients also are removed. To obviate these difficulties, foodstuffs might be grown lacking these nutrients. Although small scale water cultures have been used to show the necessity of certain trace elements in plants, the use of large-scale water cultures of the same chemical purity to grow food for animals has never been described.[3]

Many plants grow well without halogens or sodium, and improved techniques for growing such plants during the past nine years have been achieved by McClendon and will be described elsewhere. By the use of these techniques roentgen studies of the effect of fluorine-free diets on the osseous and dental structures of the rat were made possible.

METHOD

In all rat feeding experiments, litter-mate albino rats at weaning (21 days old) were used, and divided into approximately equal numbers of experimental animals and controls. The controls were either on the fluorine-free diet with 10 parts per million fluorine as fluoride added to to drinking water, or they were on an identical regimen except that the diets were derived from plants grown in soil instead of in fluorine-free water.

The water-cultured diets were made up of yellow corn, sunflower seeds, leaves and yeast, all grown in fluorine-free water, with additions of fluorine-free chemicals: glucose, corn oil, cod liver oil (containing 9 parts per million of iodine), and sodium chloride. Since rats on deficient fluorine diets did not grow at normal rates, 0.07 per cent methionine, 0.1 per cent cystine and 0.1 per cent lysine were added to diets in some experiments. To the diet of others fed on fluorine-free foodstuffs, the purest reagent calcium citrate obtainable was added, even though this resulted in the addition of 0.004 part per million of fluorine to the whole diet. Determination of fluorine content of the food and of the teeth were done by the method of McClendon and Foster.[4] Roentgen studies were done at the end of the experiments.

RESULTS

In 16 rats, the fluorine-free diets produced dental caries in 84 per cent of all the molar teeth. The entire crowns of the molar teeth disappeared frequently (Table 1). In those experiments where 0.004 part per million of fluorine were added to the diet, dental caries also appeared in all the molars.

When 10 parts per million of fluorine in the drinking water were added to the diet of those rats fed the fluorine-free foodstuffs, dental caries appeared in only 6 per cent of the molars.

On the other hand, the soil grown foodstuffs, with natural content of fluorine, allowed caries to appear in 23 per cent of the molar teeth.

Animals fed on water-cultured fluorine-free foods tended to die within two to three months and this premature death could be

TABLE I

DENTAL CARIES IN RATS FED VARYING CONCENTRATIONS OF FLUORINE IN FOOD AND WATER

	No. Rats	No. Carious Molars	Percentage Carious Molars	Percentage Fluorine in Molars
Rats on water-cultured fluorine-free diet and fluorine-free water	6	65	84	0.01
Rats on fluorine-free diet and water containing fluorine 10 ppm.	3	2	6	0.03
Rats on fluorine-free diet supplemented with 10 cc. milk containing 1 mg. fluorine	3	9	25	0.02
Rats fed soil-grown foods and fluorine-free water	4	11	23	0.02

partially delayed by a feeding of 10 cc. milk containing 1 mg. of fluorine.

The fluorine content of the molar teeth roots in the rats fed on fluorine-free diets contained 0.01 per cent; in the molar teeth roots of those rats given the milk fluorine supplement, the concentration of fluorine was found elevated to 0.02 per cent. This effect was observed sixteen days after the milk-fluorine supplement had been given only once. The teeth of the rats fed a fluorine-free diet but given water containing 10 ppm. of fluorine, revealed a dental content of 0.03 per cent of fluorine.

The urine and feces of all the rats on a fluorine-free diet revealed no traces of fluorine, indicating that the inherited fluorine was retained.

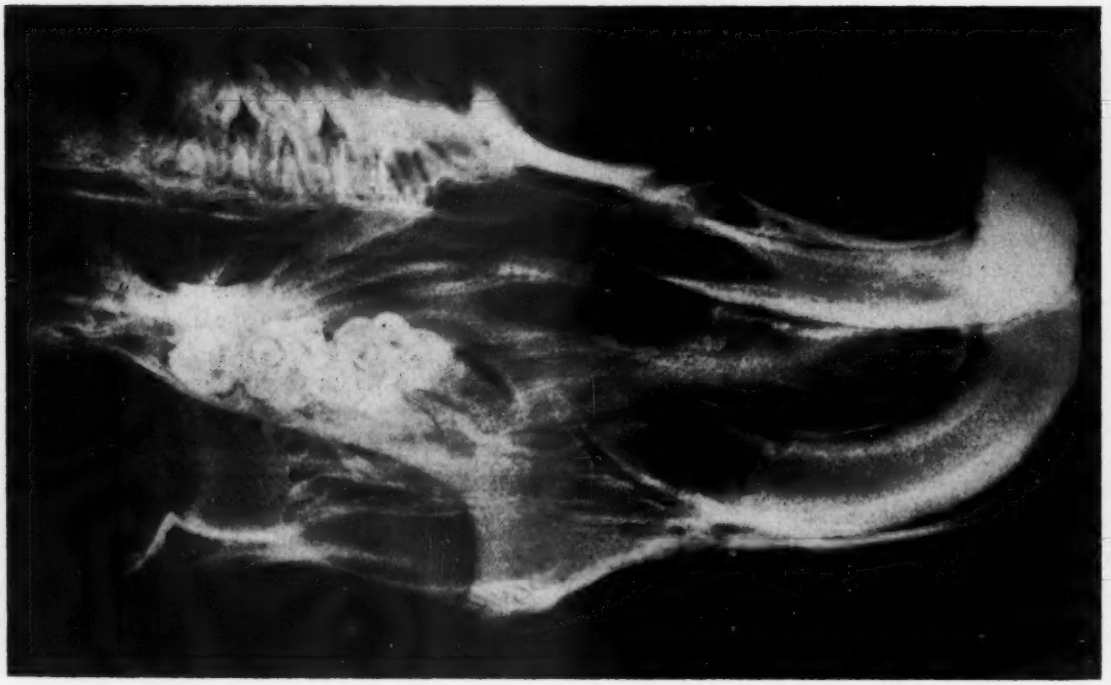

FIG. 1. Healthy teeth and maxilla of rat on water-cultured fluorine-free diet and water containing 10 ppm. fluorine. (Enlarged 5×.)

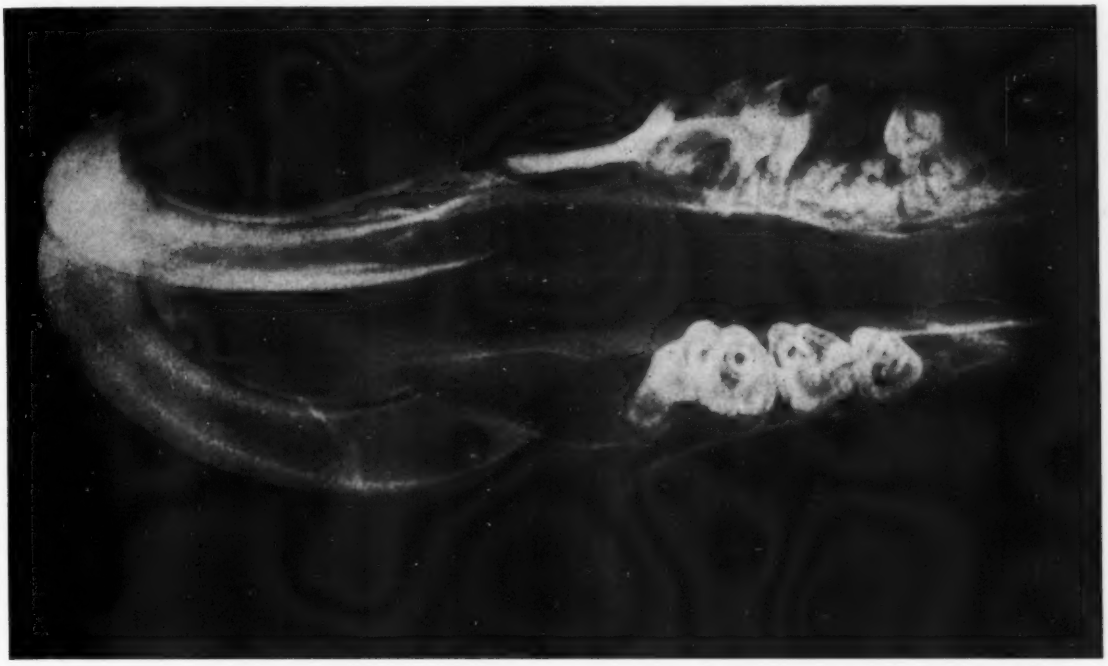

Fig. 2. Extensive caries of molars and thickening of the cementum in maxilla of rat, a litter mate of the rat in Figure 1, but fed on a water-cultured fluorine-free diet and on water containing no fluorine.

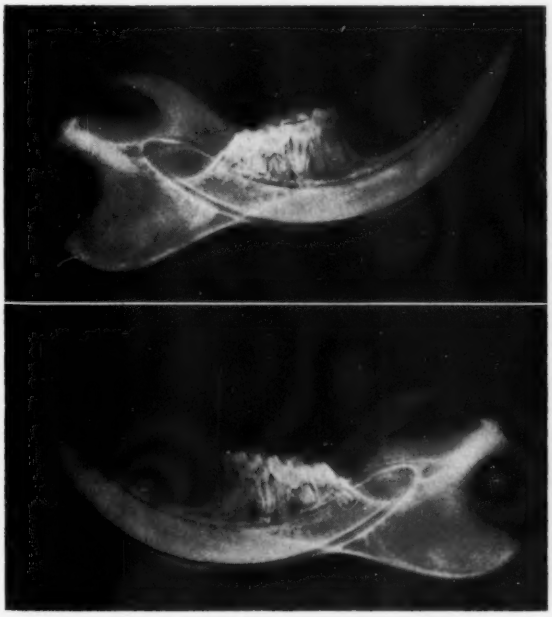

Fig. 3. Healthy teeth and mandible of rat fed soil-cultured food and tap water. (Enlarged 3×.)

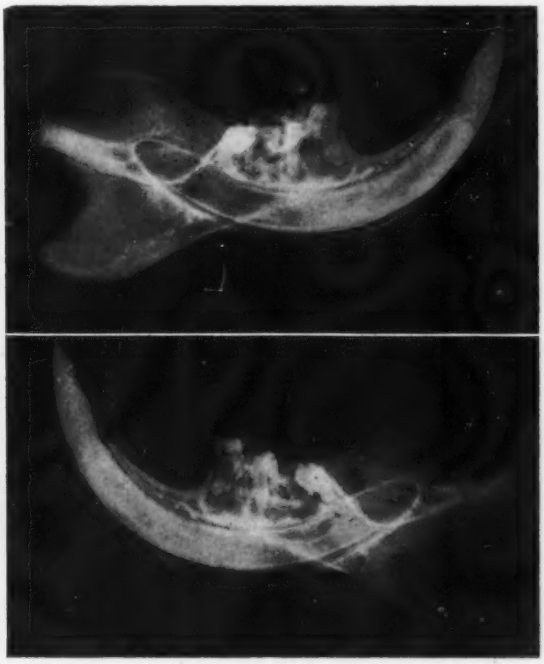

Fig. 4. Carious teeth and periodontoclasia in mandible of litter mate of rat in Figure 3, fed water-cultured fluorine-free food and fluorine-free water.

The roentgen examinations revealed extensive caries of the molars in those rats on the water-cultured fluorine-free diets. Much periodontoclasia was present in the molar areas. These changes contrasted sharply with the healthy teeth and calcification in the jaws of the rats fed supplements of 10 ppm. fluorine in the drinking water. The caries of the molars in those rats fed on soil cultured foods was minimal (Fig. 1 to 4).

DISCUSSION

The necessity of any element for mammals may be shown by an absence or by a sufficiently low concentration of the element in the diet. If the element is transmitted from the mother through the placenta and milk, it would be desirable to continue the diet through two generations. A number of female rats fed a fluorine-free diet and mated to normal males did not produce viable offspring. Therefore we suspect that fluorine is necessary in the diet of the rat. The teeth of our rats on a fluorine-free diet contained some fluorine inherited from the mother. Since the chemical tests showed a lower concentration of fluorine in the dentine of these animals, and since no excretion of fluorine was noted in the urine or feces, this small concentration of maternally derived fluorine seems to be fixed or retained. If the absence of fluorine in food uniformly produces dental caries and periodontoclasia, as our experiments would indicate, then the fluorine content of foodstuffs would seem to merit as much attention as the fluorine content of drinking water. Numerous observations indicate that fluorination of community drinking water with 1 ppm. of fluorine usually reduces the incidence of dental caries about 50 per cent. This also would suggest that our knowledge concerning the varying degrees of the fluorine content in our foodstuffs merits more study and control.

SUMMARY

Dental caries and periodontoclasia were produced almost uniformly in rats fed on a water-cultured fluorine-free diet and fluorine-free water. This caries could be prevented by the addition of fluorine to drinking water.

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We are indebted to William C. Foster for fluorine analyses; to the Aluminum Company of America and Lever Bros. for research grants, and to J. C. Anderson of Rutgers University for hybrid corn seed.

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Vol. 71, No. 6

PHYSICAL FACTORS IN THE USE OF COBALT 60 IN INTERSTITIAL AND INTRACAVITARY THERAPY*

By GILBERT H. FLETCHER, M.D., PETER WOOTTON, B.Sc., WILLIAM H. STOREY, B.A., *and* ROBERT J. SHALEK, PH.D.

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THE problem of using cobalt 60 in lieu of radium for interstitial, intracavitary, and surface applications is twofold:

(1) Determination of the optimal design of capsules and needles.
(2) Conversion and adaptation of systems of dosimetry developed for radium.

Due to the softness of cobalt 60 beta rays, a small thickness of steel or nylon is sufficient for their complete absorption. The steel or nylon produces fewer secondary electrons than the gold or platinum necessary for radium screening. It was thought that thinner needles would be less traumatic to the tissues, so that steel needles and nylon tubing of lesser diameter and shorter dead ends than platinum needles (less than the average 5 mm. of the platinum needles) have met with widespread use. The same applies for more intense sources used in tandems or applicators.

Once the beta rays are filtered, radium (0.8 mev. E.W.L.) and cobalt 60 (1.25 mev.) are gamma-ray emitters which would be expected to be similar in biologicale effectiveness. In the early clinical work, it was assumed that differences in diameters, oblique filtration, and thicknesses of dead ends would not be clinically significant.[7,8,9,10] Tables for linear sources[13] and the Paterson-Parker system were used for cobalt 60 therapy, after conversion by the factor

$$\frac{\text{gamma r 1 mg. radium 0.5 mm. Pt}}{\text{gamma r 1 mc. Co}^{60}\text{ unfiltered}} \textit{ i.e., } \frac{0.84}{1.356}.$$

Clinical users have then delivered alleged doses similar to those they would have used for radium, and some have stated that reactions were similar to those of radium.[1,9] However, reactions observed in random clinical use are not a sensitive and reliable test to evaluate rather small differences (up to 20 per cent) in dosage levels and integral doses.

Experimental work on rabbit skin[8] has cast doubt as to the validity of the procedure. It is desirable, therefore, to investigate the physical factors which are directly connected with the use of cobalt 60 in the various modalities of gamma-ray therapy, and determine whether radium and cobalt differ in any major respect.

The physical factors which must be considered are:

(1) The effective absorption of cobalt 60 and radium in a scattering medium.
(2) The ion density distribution.
(3) The volume distribution of radiation around linear sources.

The ratio (dose rate in water/dose rate in air) for radium and cobalt 60 has now been studied for distances encountered in either interstitial, intracavitary or surface application therapy by two different groups with agreement.[16,17] The behaviors of cobalt 60 and radium gamma rays are similar in a water phantom. This means that a system calculated in air, but often applied in tissue, such as the Paterson-Parker or Quimby systems for radium will contain similar errors in their cobalt and radium applications; therefore, no difference between the end results from the two materials can be attributed to this factor.

The biological efficiency of various levels of energy has been related to the ion density distribution produced in water. It has been shown that the ion density produced in

* Presented at the Thirty-fifth Annual Meeting, American Radium Society, St. Louis, Mo., April 20–22 1953.

TABLE I A, B

THE DOSE RATES AROUND COBALT AND RADIUM SOURCES OF VARIOUS ACTIVE LENGTHS AND FILTRATIONS WERE MEASURED. THE DATA FOR ONE RADIUM AND ONE COBALT NEEDLE ARE TABULATED ABOVE. THE DOSE RATES WERE CALCULATED USING SIEVERT INTEGRALS[12] AND GOOD AGREEMENT OBTAINED, EXCEPT IN THE ZONES BETA AND GAMMA, WHICH ARE DIFFICULT TO TREAT MATHEMATICALLY. NO ATTEMPT WAS MADE TO CALCULATE THE DOSE RATE ALONG THE AXIS OF THE NEEDLE

Distance ⊥ to Axis (cm)	Distance from Mid-Point Along Axis (cm) 0	1	2	3	4	
0.0	Needle — —			1.56	.65	γ Zone
0.5	21.2 (21.2)	18.6 (18.4)	5.6 (5.1)	1.8 (1.5)	.8 (.65)	β Zone
1.0	8.4 (8.5)	7.1 (7.1)	3.8 (3.4)	1.7 (1.4)	.74 (.7)	
2.0	2.8 (2.8)	2.5 (2.5)	1.7 (1.7)	1.0 (1.1)	.58 (.68)	
3.0	1.34 (1.33)	1.3 (1.2)	1.00 (1.00)	.74 (.74)	.48 (.53)	

( ) = Calculated

2.94 cm Active Length
1.6 mm Diameter
0.3 mm Steel Sheath
1.0 mm Diameter

Co^{60}

A

Distance ⊥ to Axis (cm)	Distance from Mid-Point Along Axis (cm) 0	1	2	3	4	
0.0	Needle — —			.46	.174	γ Zone
0.5	11.1 (11.1)	11.5 (12.5)	2.9 (3.0)	.78 (.72)	.34 (.28)	β Zone
1.0	5.0 (5.05)	4.3 (4.4)	2.1 (2.1)	.81 (.84)	.42 (.42)	
2.0	1.7 (1.7)	1.5 (1.5)	1.10 (1.00)	.62 (.65)	.38 (.40)	
3.0	.81 (.84)	.81 (.77)	.62 (.61)	.50 (.46)	.32 (.32)	

( ) = Calculated

2.89 cm Active Length
1.82 mm Ext. Diameter
0.6 mm Wall Thickness
Two cells 1.27 cm each
3.5 mm Separation

Ra

B

water by cobalt and radium gamma radiation is substantially equal,[4] and on these grounds it is unlikely that there would be a difference in the biological effectiveness of the two agencies. Therefore, before it can be concluded from observations obtained in interstitital implantations or surface applications either in animals or humans that a difference in biological efficiency exists, a careful study of the dosimetry of cobalt 60 and radium sources used is essential, not only within the area treated but also around it as the severity of reactions is a function of the total volume dose and increases with it.[5]

We therefore investigated the following points:

(1) Volume distribution of dose rates round linear sources as customarily used, *i.e.*, 16-gauge cobalt 60 needles with short dead ends and radium needles or tubes with discontinuous cell loading. The types of sources employed in the current study are illustrated in Figure 1.

(2) Influence of any differences found on the pattern of dose rates for implantations of cobalt and radium.

(3) Attempt to evaluate the clinical significance of the findings.

(4) Suggest modifications of design of the containers (tubes or needles), and the current radium treatment systems, to adopt them for cobalt therapy (Table II).

The dose rate distribution around radium and cobalt sources can be calculated by such mathematical methods as that of Sievert.[14] The dose rate at the surface of the needles obtained by considering the activity as concentrated on the central axis and applying the Sievert formulas may be questioned owing to the unusual geometry. Accordingly, the dose rate at the surface of the needles was calculated by considering the sources as composed of elemental discs and integrating these contributions graphically, all filtration effects ignored. The results so obtained were compared with those from considering the activity as con-

centrated on the central axis, again all filtration effects ignored. It was found that, provided the sources were more than 1 cm. in length, the two methods yielded results within 5 per cent of one another, the integrated disc contribution always yielding the higher value of cobalt/radium ratio. If these calculations are confined to the zone designated as the alpha zone (Fig. 2) and full cognizance taken of the cell loading of the radium sources, then good agreement is obtained with direct measurements in zone α (Table 1). Measurements were, however, thought to be desirable because:

(1) The absorption coefficients employed in the calculation were narrow beam absorption coefficients[6] and certain assumptions were made about the self-absorption in the cobalt sources, namely that the entire activity of the cobalt could be considered as being concentrated along an axial line and being filtered through the wall of a cylinder of geometrically similar cobalt inside a cylinder of steel.

(2) The zones marked beta and gamma on Figure 2 are difficult to treat, owing to the problem of making valid simplifications of the shape of the point and eyelet of the needles. It is noticeable that there the measurements and the calculated values do not agree so well.

TABLE II

THE RATIO OF VOLUME ENCLOSED BY THE ISODOSE SURFACES OF 2.5, 5, AND 10 ROENTGENS PER HOUR WERE CALCULATED FROM THE ISODOSE CURVES, ASSUMING THE SURFACES TO BE SURFACES OF REVOLUTION OF THESE CURVES. THE RESULTS ARE TABULATED ABOVE. IT IS TO BE NOTED THAT THE LARGEST DIFFERENCES BETWEEN COBALT AND RADIUM OCCUR WHEN THE END EFFECTS ARE INCLUDED IN THE VOLUMES, *e.g.*, 2.5 R SURFACE

Isodose Curve	2½ r/h	5 r/h	10 r/h
Ratio $\frac{\text{Cobalt}}{\text{Radium}}$	1·2	1·14	1·12

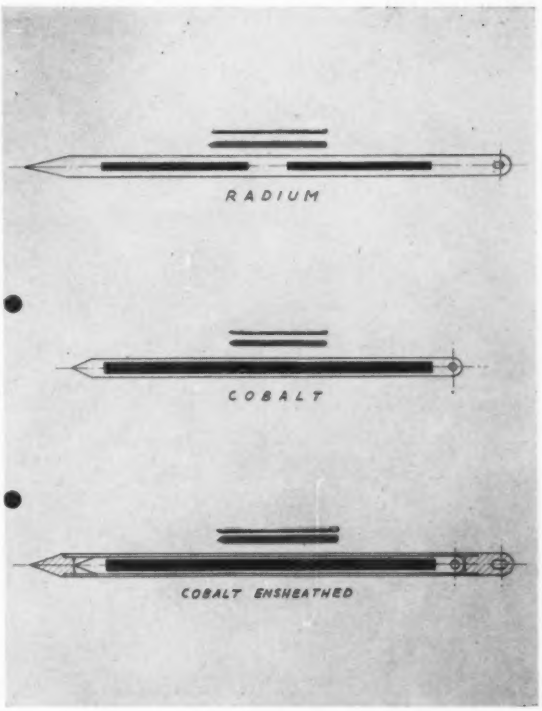


FIG. 1. The sources used in the experiments were the standard radium, cell-loaded, platinum-sheathed needles, as commercially manufactured, and cobalt continuously filled steel-sheathed 16-gauge needles as issued by the Eldorado Company. Extra sheaths for the latter were formed from 14-gauge blood transfusion needles in order to make the same over-all length and slightly greater diameter (2.1 mm. compared with 1.82 mm.) than the radium needles. The sources are illustrated above.

(3) In the study of the implants, the dose rate around the implants in the plane of the needles is difficult to deal with theoretically, owing to the filtration through several cylindrical filters that would be involved. Similarly, the effect of crossing needles under or over the main implant is better measured than calculated.

Apparatus was assembled to perform these measurements. The detecting element was a wavelength independent scintillation crystal (anthracene), the light output from which was amplified by a photomultiplier tube whose resulting current was measured by a sensitive galvanometer.

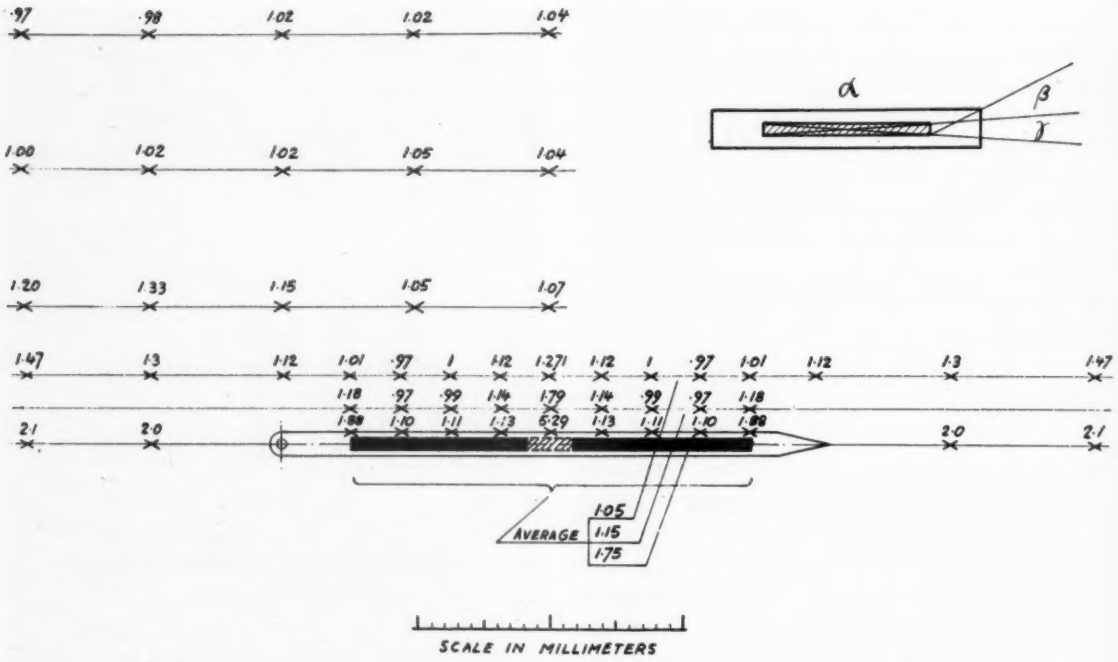


FIG. 2. The mathematical treatment of the intensity around linear radioactive sources depends on the situation of the point considered relative to the geometry of the source and its sheathing. The area can best be divided into three zones labelled in the drawing: alpha, beta, and gamma (see upper right hand corner of the figure). In zone alpha, filtration can be considered to be through a cylinder extending to infinity along its axis; in zone beta, only part of the source can be treated in such a way, part is filtered through the end wall of the container. In zone gamma, all is filtered through the end wall in addition to self filtration. Zones beta and gamma are difficult to deal with mathematically, because of the problem of simplifying, in a satisfactory fashion, the geometry of the points and eyelets of the sources.

The ratio of dose rates cobalt/radium for sources delivering identical dose rates at 1 meter are shown in diagrammatic form. Those at 0.25 cm. within the active length of the sources and on the surface of the needles were calculated using the formulae that are justified by results shown in Table 1. The surface dose rates are those at the surfaces of the actual needles, 0.91 mm. from the axis in the radium needles, and 0.8 mm. in the case of cobalt; the cell loading was used in the calculations.

The system was tested for linearity both with different intensities of radium and cobalt gamma radiation and for wavelength independence by comparison with an air-wall chamber through the radium and cobalt equivalent energy spectrum.

The method of location of the source relative to the detector was to locate the detector at the origin of a grid system in which the source could be moved from point to point at 0.5 cm. intervals. The mount and grid systems were so designed that the source could be accurately replaced. A microscope stage adjustment was utilized, so as to locate the detector accurately at the origin of the grid system (Fig. 3).

LINEAR SOURCES

The agreement between measurement and theory for linear sources can be seen in Table 1. Isodose curves were also drawn round linear sources by means of an isodose recorder[3] (Fig. 4). Typical curves appear in Figure 5. The greatest difference between radium and cobalt can be seen around the ends. Taking the isodose curves around sources of similar geometry and activity, an estimate was made of the volume enclosed by corresponding isodose surfaces. The ratio of the volume is shown in Table II. The effects of oblique filtration are not so evident in the isodose curves but are more apparent in Figure 2 which illustrates the ratio Co/Ra for sources which deliver

identical dose ratios at 1 meter. The ratio is shown for points along the axis of the needles, the surface of the needles and surfaces 0.25, 0.5, 1, 2, and 3 cm. distant from the needles and parallel to them.

The values at 0.5 cm. and at greater distances are averaged readings, those at 0.25 cm. and at the surface of the needles are obtained by calculation.

The cell loading of the radium gives rise to wide variations in the ratio at various points along the needles. To estimate some trends, arithmetic mean values of 9 points along the active lengths are also offered in Figure 2.

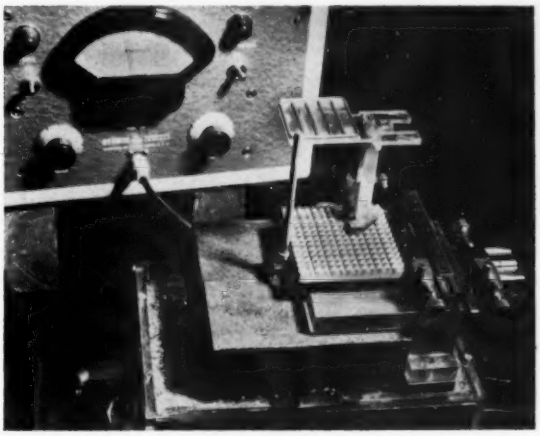


Fig. 3. The apparatus consists of a means of accurately locating the movable source relative to a fixed, wavelength independent detector. This was accomplished by mounting the source on a three-footed stand, the ball feet of which rest in V grooves accurately milled at 0.5 cm. intervals in a thick aluminum block. This block could be moved on a microscopic stage so that the detector coincided with the origin of the grid system in which the source moved. The anthracene crystal detector, 3 mm. in diameter, thickness 2 mm., is housed in an internally polished aluminum tube acting as a light pipe into a type 931A photomultiplier tube. The cathode of the tube was protected from direct radiation by a 5 cm. lead block and cooled by solid carbon dioxide. The signal was measured by the photo tube current monitored by a galvanometer. After all runs, the crystal was removed and the source replaced in the previous geometry. The tube current was then noted and deducted from previous readings so that readings due to scintillation in the crystal alone were recorded. The apparatus was tested for linearity both with regard to quantity at a fixed wavelength and with changes in wavelength and was found to be linear within limits of accuracy of reading the galvanometer scale.

Fig. 4. Isodose curves around separate linear sources and around arrays of such sources were plotted by means of an isodose recorder. The signal from the wavelength independent detector (anthracene crystal) is fed to a Brown amplifier which tracks it toward or away from the radioactive sources so as to maintain it on a constant preselected gamma-ray intensity as the source is rotated. The movement of the detector is followed by a pen tracing on a paper mounted on a table which rotates with the source. The pen thus traces isodose curves. The plane to be explored is chosen by raising or lowering the source or by altering its angulation in the holder.

For the purpose of discussion it is convenient to consider four areas: (1) bounded by the active ends of the needle and extending from the 0.25 cm. line outwards, (2) bounded by the active end and extending around to the axis of the needle, (3) along the axis of the needle, (4) proximity of the needle surface.

In area (1) it can be seen that as movement is made toward the sources, the ratio Co/Ra increases such that the average value at 0.5 cm. distance = 1.05, at 0.25 cm. = 1.15. In area (2), the cell loading and

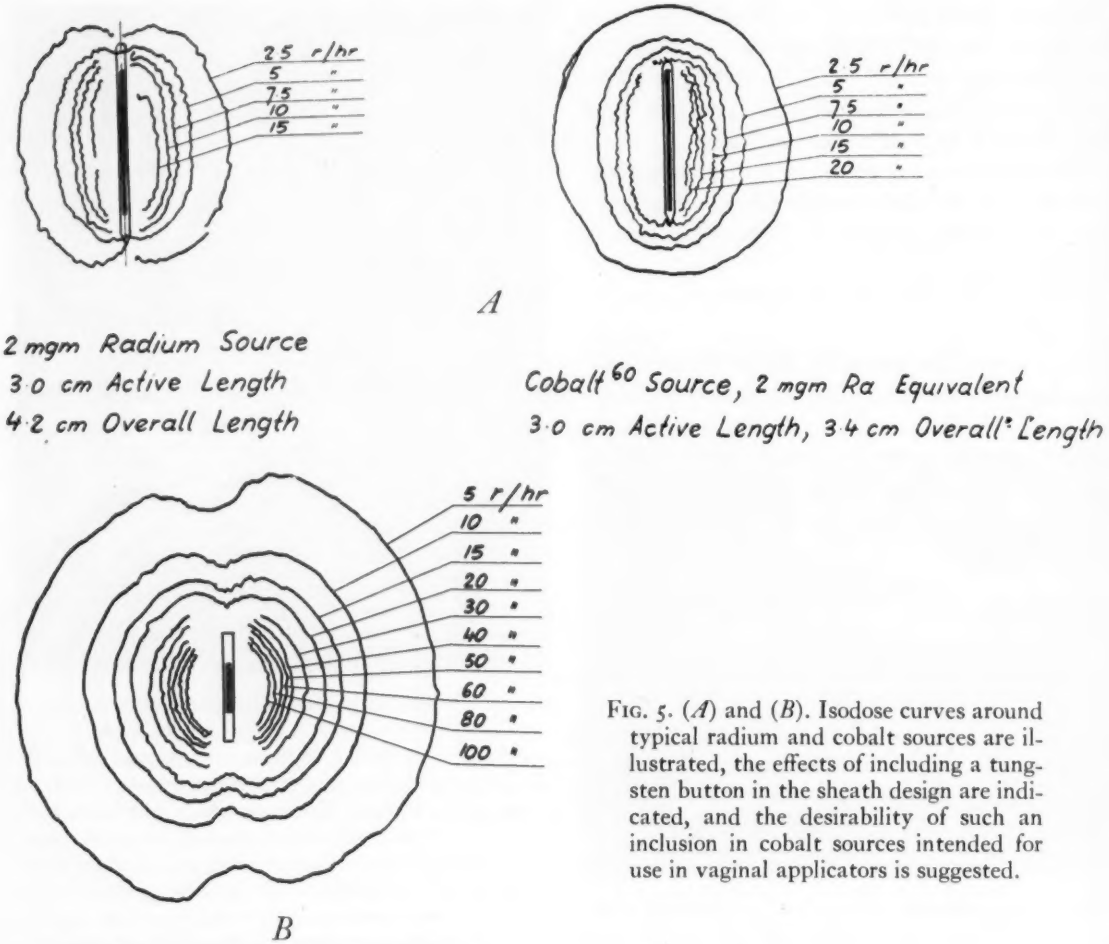


FIG. 5. (*A*) and (*B*). Isodose curves around typical radium and cobalt sources are illustrated, the effects of including a tungsten button in the sheath design are indicated, and the desirability of such an inclusion in cobalt sources intended for use in vaginal applicators is suggested.

therefore effective displacement of activity toward the ends of the radium needles, combined with the effects of the heavy sheaths causes a range of values between 0.97 and 1.49, *i.e.*, the cobalt delivers between 3 per cent less to 47 per cent more radiation than the equivalent radium; the delivery of greater doses predominates. In area (3), the cobalt needle delivers twice as much radiation. Extrapolation of the values back to the site of the eyelets shows that approximately three times as much radiation is experienced at the site of the cobalt eyelet as is received at the radium eyelet, due to difference in length of dead ends.

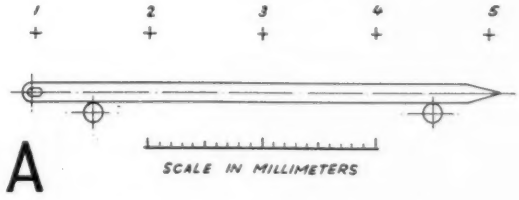
The surface of the needles differs in distance from the effective active axis of the source. The radium needle has a diameter of 1.82 mm., and the cobalt a diameter of 1.6 mm. The average value of Co/Ra ratio at the surface is 1.75/1. An experimental check on the surface dose rate was attempted by chemical methods. Measurements were made on the energy absorbed in a tissue-like medium (dilute acid solution of ferrous ammonium sulfate) diameter 4 mm. and length 3 cm. surrounded by a full-scattering medium and with a radium

TABLE III A, B

THE DOSE RATE WAS MEASURED IN A PLANE 0.5 CM. AWAY FROM AN IMPLANT 3 BY 3 CM. AND CONSTRUCTED ACCORDING TO THE PATERSON-PARKER SYSTEM, USING RADIUM AND COBALT SOURCES OF 2 MILLIGRAMS AND 1 MILLIGRAM EQUIVALANT ACTIVITY. THE IMPLANT WAS CROSSED ON THE SIDE OPPOSITE TO THE PLANE OF MEASUREMENT. THE DOSE RATES WERE COMPUTED FROM THE MEASUREMENTS TABULATED IN DIAGRAM I FOR INDIVIDUAL NEEDLES AND ARE OFFERED ABOVE FOR COMPARISON. THE OPERATIONS WERE PERFORMED ALONG THE TWO RIGHT BISECTORS OF THE IMPLANT. IN ONE CASE, THE MEASUREMENTS RUN ACROSS THE CENTRAL NEEDLES, IN THE OTHER ALONG THE LENGTH OF THE NEEDLES

	Nature of Data	1	2	3	4	5
Co	Calculated	32.4	52.17	54.20	52.17	32.4
Co	Measured	33.8	56.0	58.0	56.0	33.8
Ra	Calculated	30.2	49.32	50.08	49.32	30.2
Ra	Measured	26.6	48.8	48.25	48.8	26.6

Paterson/Parker Dose Rates: $Ra_{Co^{60}}$ 54 r/hr 55.3 •

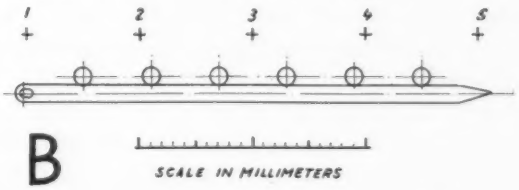


A

SCALE IN MILLIMETERS

	Nature of Data	1	2	3	4	5
Co	Calculated	33.5	54.7	54.2	54.7	33.5
Co	Measured	33.6	56.1	58.0	56.1	33.6
Ra	Calculated	25.7	52	50.0	52	28.7
Ra	Measured	28.1	47	49.0	47	28.1

Paterson/Parker Dose Rates: $Ra_{Co^{60}}$ 54 r/hr 55.3 •



B

SCALE IN MILLIMETERS

source active length 3 cm. coaxial with it. The experiment was repeated with the cobalt sources. The formation of the ferric ion was the method of estimate employed and yielded a Co/Ra ratio of 1.5/1.

It can therefore be seen that, in addition to complete beta-ray filtration there are other relevant factors in the design of the radium and cobalt sources. Among these are:

(1) Differences in diameter of the needles, producing differences in surface intensity. The surface dose rates for cobalt sources of various designs taking the average of an equivalent radium needle as unity may be summarized as follows:

(a) 19-gauge.....3.0
(b) Nylon thread.....2.01
(c) 16-gauge.....1.75
(d) 14-gauge.....1.15

(2) Length of dead ends of needles; dose rates at the eyelet of commercial cobalt and standard radium needles differ by a factor of 3.

SINGLE PLANE IMPLANTS

To investigate the significance of differences in dosage rates in the usual patterns of interstitial gamma-ray therapy, single plane implants were chosen because this class of implants is simple to study and very widely used. The distribution of radium or cobalt 60 followed the Paterson-Parker rules, the outer needles being of full strength and the needles in the area half strength. The actual values of both radium and cobalt were checked by use of a Lauritzen electroscope. The needles, both cobalt and radium, were checked for uniformity of load by crystal measurement and radioautograph.

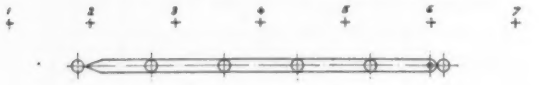
In our experience, some of the cobalt sources are not always of uniform activity along their length and across their diameter. It would appear, therefore, that the units that had been loaded into such

TABLE IV A, B

THE OPERATIONS PERFORMED FOR THE 3 BY 3 CM. IMPLANT WERE REPEATED FOR THE 4.3 BY 4.3 CM. IMPLANT AND ARE PRESENTED FOR COMPARISON ABOVE. IN THIS CASE, THE CROSSING NEEDLES BEING AT THE PHYSICAL ENDS OF THE NEEDLES, ALL ARE IN THE SAME PLANE

	Nature of Data	1	2	3	4	5	6	7
Co⁶⁰	Calculated	19.2	42.0	39.5	38.5	39.5	42	19.2
	Average Measurement	17.9	41.5	39.75	40.5	39.75	41.5	17.9
Ra	Calculated	17.3	36.5	36.7	35.7	36.7	36.5	17.3
	Average Measurement	16.1	34.5	34.25	34.0	34.25	34.5	16.1

Paterson/Parker Dose Rates: Ra 34.2 r/h Co⁶⁰ 35 r/h



A

SCALE IN MILLIMETERS

	Nature of Data	1	2	3	4	5	6	7
Co⁶⁰	Calculated	18.0	40.25	38.5	38.5	38.5	40.25	18.0
	Average Measurement	16.75	37.5	38.9	40.25	38.9	37.5	16.75
Ra	Calculated	16.4	32.3	35.7	35.7	35.7	32.3	16.4
	Average Measurement	17.0	31.4	33.4	34.0	33.4	31.4	17.0

Paterson/Parker Dose Rates: Ra 34.2 r/h Co⁶⁰ 35 r/h

B

SCALE IN MILLIMETERS

needles had not been matched as closely as may be desirable nor were they uniformly activated.

The implants were formed by mounting the needles on plane sheets of plexiglass as thin as were compatible with rigidity. V-shaped grooves were milled at accurately located intervals on these sheets of plastic and the needles waxed in position in these grooves.

Measurements were performed with the same apparatus as was used for the needles, and were taken:

(1) In a plane parallel to that of the implant at 0.5 cm. separation.
(2) In the plane of the implant in the area bordering the implant.

The first implant investigated was 3 by 3 cm., *i.e.*, the crossing needles were at the level of the active ends.

This implies that two needles are not in the plane of the rest of the implant. The effect of the position of these needles was investigated.

An implant 4.3 by 4.3 cm. was next chosen. This allows the use of the same needles as before, the crossing being performed at the physical ends of the radium needles; therefore all needles are in the same plane. Same size implants were also explored when one crossing needle was omitted. All experiments were performed for cobalt and radium, with identical distances between needles.

The data were tested for agreement with the results obtained by summing up the effects of the individual needles at various points across the perpendicular bisectors of the plane 0.5 cm. away from that of the implant. The correlation can be seen in Tables III and IV.

The ratios Co/Ra at various points given in Figures 6 and 7 are corrected to those for implants delivering dose rates at 1 meter.

It can be seen from Figures 5 and 6 that inside the treatment zone delineated by the peripheral needles nominally equal quantities of cobalt and radium yield dose rates which differ by 5 per cent in the plane of Paterson-Parker calculation (*i.e.*, 0.5 cm. plane). The difference would be expected to increase on approaching the plane of the implant. Considering still the plane 0.5 cm. away from the implant and moving to the area adjoining the implant, the ratio Co/Ra dose rate rises to an average value of 1.15.

In the plane of the implant, the difference inside the treatment zone is likely to be of the order of 15 per cent between needles and approaching 75 per cent at the

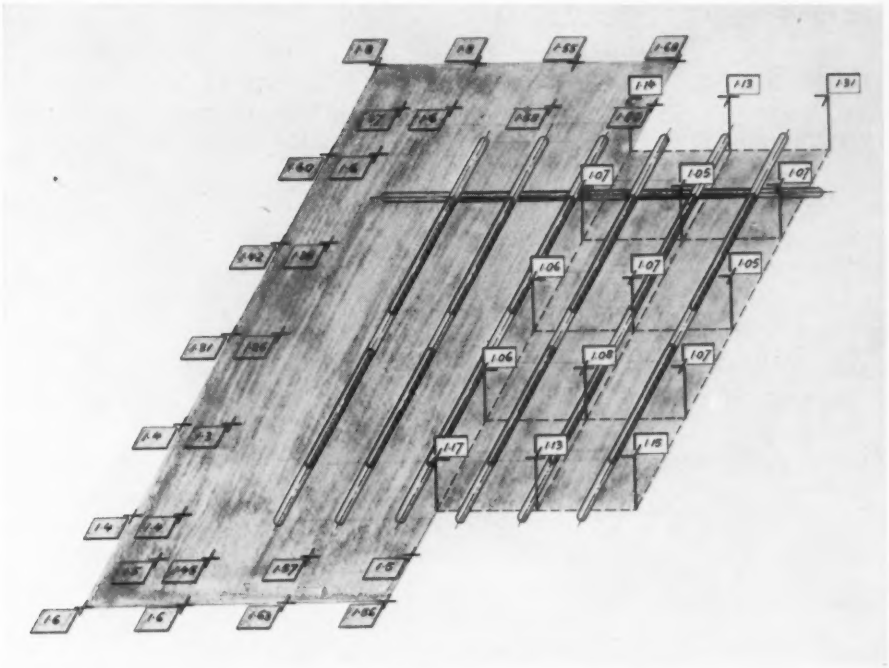


Fig. 6. The ratio cobalt/radium dose rates are shown in the above diagram for an implant 3 by 3 cm., one end uncrossed. The ratios at the crossed end may be taken as representative for a fully crossed implant. It can be seen that in the normal plane of Paterson-Parker calculations (0.5 cm. from the implant) inside the treatment area the cobalt delivers 5 per cent more than its equivalent radium. The difference increases outside the treatment zone and would be expected to increase on approaching the plane of the implant. In the plane of the implant itself the difference between needles is of the order of 15 per cent while the ratio at the surface of the needles (see Fig. 2) is 1.75/1. Outside the treatment zone the average value of the cobalt/radium ratio is 1.6 to 1.

At the uncrossed end the ratio cobalt/radium falls slightly but cobalt still delivers 50 per cent more radiation in the plane of the implant and some 15 per cent more in the plane normally used for calculation.

The ratio cobalt/radium is not much affected by the plane in which the crossing needles pass but the absolute value of the dose rate is some 8 per cent higher on the crossing needle side. For values and comparison with Paterson-Parker, see text.

surface of the needles. Outside the treatment zone the dose rate for cobalt is 30–80 per cent greater than that due to radium implant in the case of the smaller area and 15–50 per cent greater in the case of the larger area. If 7,000 roentgens are delivered in the therapeutic plane, the average value for the absolute dose rate for the smaller implant in the fringe area 1 cm. from the peripheral needles is 1,600 roentgens for radium, 2,500 roentgens for cobalt. At 1.5 cm. it is 1,000 roentgens for radium and 1,600 roentgens for cobalt. In the larger implant, the corresponding values are 2,400 roentgens for radium compared to 2,800 roentgens for cobalt and 1,500 roentgens for radium compared to 1,800 roentgens for cobalt.

The reason for these variations with area in different zones is plainly due to the relative importance of the contributions from needles in the implant other than the immediately neighboring needle. The importance varies with the dimensions of the implant, *i.e.*, the distance between these other needles and the point under consideration, the filtration through multiple platinum cylinders remaining essentially constant. It is to be expected, therefore, that the disparity between cobalt and radium in the fringe areas will be large for small implants becoming smaller as the implant

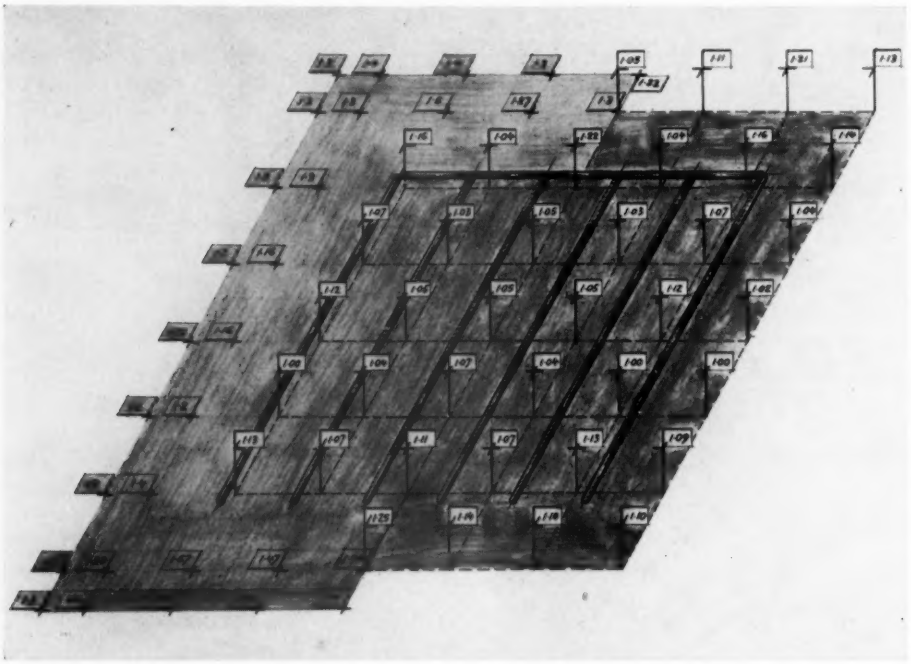


FIG. 7. The ratio cobalt/radium dose rates are shown in the above diagrams for an implant 4.3 by 4.3 cm., one end uncrossed. The ratios at the crossed end may be taken as representative for a fully crossed implant. The pattern of ratios in the 0.5 cm. calculation plane follows a similar pattern to that of the 3 by 3 cm. implant (Fig. 6). In the fringe areas in the plane of the implant the average ratio is 1.35/1.

As at the uncrossed end the pattern is again similar to that of the 3 by 3 cm. uncrossed end, the cobalt delivers some 50 per cent more radiation than the radium. For range of dose rates of the area averages and comparison with Paterson-Parker values, see text.

increases in size until it assumes approximately a constant value.

APPLICATION OF PATERSON-PARKER TABLES TO RADIUM AND COBALT 60

The Paterson-Parker tables are strictly accurate for circular implants, being adapted for the more practical square or rectangular formations. This leads to low dose rates at the corners of the implants, but if the implantations are performed according to the recommendations of the authors, these corners are not in the area it is desired to treat. Ignoring these corners, therefore, the measured dose rates in the 0.5 cm. plane in the treatment area may be summarized and compared with those obtained from use of the Paterson-Parker tables, as follows:

4.3 by 4.3 cm. Implant

COBALT:	Range of dose rate:	37 to 42 r/hr. (average = 38.6) Paterson-Parker calculated = 35
RADIUM:	Range of dose rate:	32.5 to 36.5 r/hr. (average = 35.2) Paterson-Parker calculated = 34.2

3 by 3 cm. Implant. Plane on the Opposite Side to Crossing Needle

COBALT:	Range of dose rate:	52 to 54.5 r/hr. (average = 53.63) Paterson-Parker calculated = 55.3
RADIUM:	Range of dose rate:	49.5 to 52.0 r/hr. (average = 50.20) Paterson-Parker calculated = 54.0

3 by 3 cm. Implant. Plane on the Same Side as the Crossing Needle

COBALT:	Range of dose rate:	53.5 to 60 r/hr. (average = 57.46)
		Paterson-Parker calculated = 55.3
RADIUM:	Range of dose rate:	50 to 56.5 r/hr. (average = 53.1)
		Paterson-Parker calculated = 54.0

The ratio of the Co/Ra dose rate at 1 meter for these implants was measured and found to be 1.03/1. From these results it may be concluded that within the range of experimental error of the measurements (±2 per cent) the Paterson-Parker tables yield a value for the dose rate which is within the 10 per cent clinical tolerance that the authors set up as their standard. The extreme ranges of measurement are within 10 per cent of the average value over the treatment plane within the effective treatment area. For small implants with crossing at the active ends, the absolute dosage rate is greater on the side of the crossing neeles.

If one crossing needle is omitted in the larger implant, an implant 4.3 by 3.6 cm. is then delineated by the needles and their active ends. The dose rate can now be calculated for this implant according to the Paterson-Parker system and compared to the measured dose rates over the effectively treated area. This area may be considered to start about 1/10 of the way up the 3.6 cm. sides of the implant from the uncrossed active ends. The results may be summarized:

4.3 by 3.6 cm. Implant. One End Uncrossed

COBALT:	Range of dose rate:	30 to 40 r/hr. (average = 35.8)
		Paterson-Parker calculated = 36.2
RADIUM:	Range of dose rate:	28 to 35.5 r/hr. (average = 32.5)
		Paterson-Parker calculated = 35.2

The removal of a crossing needle from the 3 by 3 cm. plane leaves a 3 by 3 cm. area still outlined, the results for this area on the side opposite to the crossing needle may be summarized as follows:

3 by 3 cm. Implant. One End Uncrossed

COBALT:	Range of dose rate:	41 to 53 r/hr. (average = 47.18)
		Paterson-Parker calculated = 49.2
RADIUM:	Range of dose rate:	37 to 48 r/hr. (average = 43.5)
		Paterson-Parker calculated = 48

The lowest dose rate, therefore, in an uncrossed implant would appear to be 20 per cent below the calculated value in the plane 0.5 cm. away from the implant, and the highest dose rate approximately 10 per cent higher, measured in the same plane. This proportion applies as much to the cobalt as to the radium. In the plane of the implant, however, the cobalt delivers a higher dose rate than the radium, as has been seen above for totally crossed implants. Uniformly loaded cobalt does not give as good a dose rate distribution as dumbbell sources (radium or cobalt) in an uncrossed implant.

SUMMARY OF STUDY OF PLANAR IMPLANTS

(1) The cobalt dose is 5 per cent higher than the radium dose in the 0.5 cm. plane (plane of calculation of Paterson-Parker) within the treatment area, and 15 per cent within the fringe area.

(2) Higher values appear closer to plane

of needles and are up to 75 per cent more for cobalt 60 at the surface of the needles.

(3) The dose rate is 30–80 per cent higher in a zone 1.5 cm. wide in the same plane and surrounding a 3 by 3 cm. implant, and is 15–50 per cent higher in a 4.3 by 4.3 cm. implant.

(4) In the small implant, the dosage rate is higher on the side of the crossing needles.

(5) Crossing or not crossing the ends does not have appreciable effect upon the ratio Co/Ra.

(6) Paterson-Parker figures are within 10 per cent of the actual measurements for radium.

(7) It may be surmised that in volume implants, double plane implants, etc., the Co/Ra ratio within the treatment area will be of the order of 1.05/1. The pattern in the zones adjacent to the implants will be similar to that observed for single plane implants, the differences being more important for smaller implants than larger ones.

CLINICAL TESTING

The physical study has shown the following:

Planar implants made with commercial 16-gauge cobalt needles differ from geometrically similar implants made with present day commercial radium needles in three ways:

(a) Increase of the unhomogeneity ratio (Dose at surface of needles/Average dose in 0.5 cm. plane of Paterson-Parker calculation). This effect is more marked with 19-gauge needles and nylon thread.

(b) Less sharp cut-off in dose rate at the edges of the therapeutic slab. This results in higher integral dose. This is more marked for small implants as the fringe area is proportionally greater to total area.

(c) Several times higher dose rates are experienced around the eyelets of cobalt needles compared with radium needles.

As the true biological effectiveness can only be evaluated if identical volume distribution is achieved, interstitial implants are not suitable for the study of the comparative biological effectiveness of the gamma rays of radium and cobalt 60 in tumors and normal tissues. The same number of roentgens must be delivered to the same areas and this can only be done with teletherapy units producing identical beams with cobalt 60 and radium sources, so that the wavelength is only variable. In addition, in the study of skin and mucous membrane reactions, attention should be paid to the depth at which electron equilibrium is attained.

From a practical clinical standpoint the important information is the ratio of cure rate to acute and late complications. Discomfort, intensity of acute epidermitis and mucositis, healing time, late atrophy of skin and mucous membranes and necrosis are the points to correlate with tumor control. This clinical testing can only be done by implantation alternately by radium and cobalt of large series of curable tumors.

Advanced, hopeless or almost hopeless cases are not suitable, due to the large volumes irradiated. The reactions (early or delayed) are too severe for comparative studies and also the follow-up is too short, as most patients will die from the evolution of uncontrolled primary lesions or metastases.

The comparative reactions of skin or mucous membranes elicited from subcutaneous or submucous radium and cobalt implants are of considerable importance in clinical use and ought to be known. However, they are not a gauge of the average tumor dose of the Paterson-Parker system, the sensitive layers (basal membrane and arteriocapillary plexuses) being closer to the needles than the plane (0.5 cm. distant) in which the array is designed to deliver the average dose calculated from the charts. Variations in distance will also be present as one cannot insert needles with an exact degree of duplication.

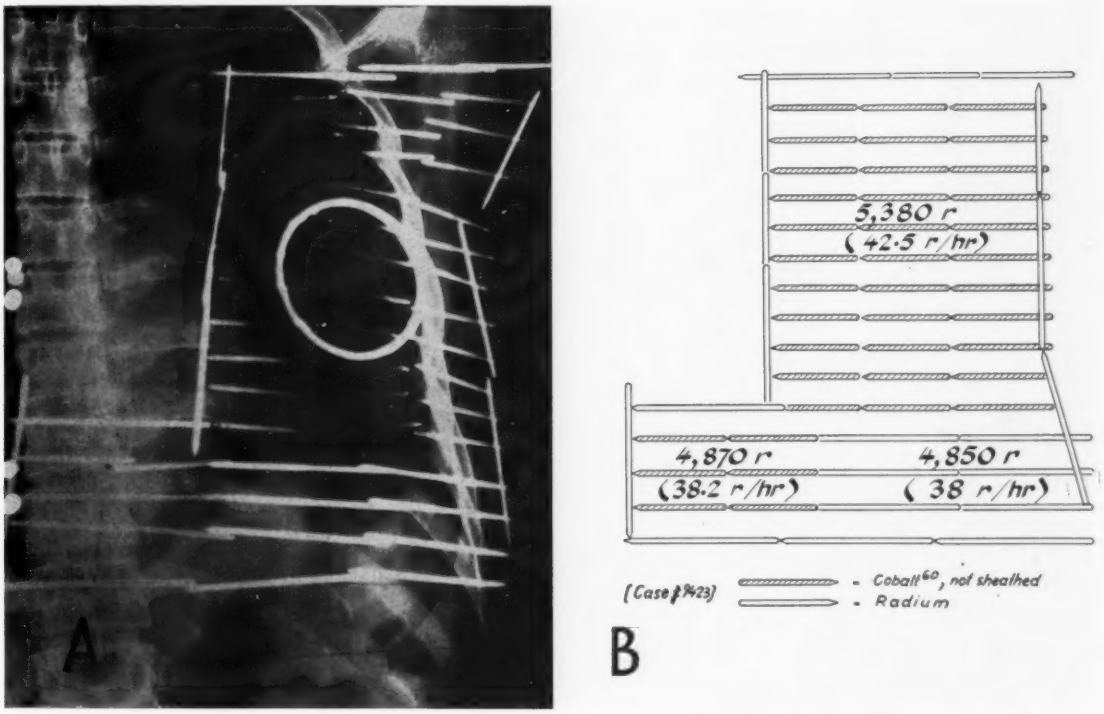


Fig. 8. (*A*) Roentgenogram. (*B*) Diagram of needles. (*C*) Color print five days after removal of needles. (*D*) Close-up color print ten days after removal of needles.

Single plane implantation of chest wall for recurrent skin nodules following simple mastectomy and inadequate irradiation (amount not known) performed elsewhere. The axilla, supraclavicular region and internal mammary chain were first treated with roentgen radiation before implantation.

The distribution of radium and cobalt sources (16-gauge) are seen on the diagram (*B*). The cobalt sources were within 2 per cent of the equivalent activity of the radium. The dose rates were calculated separately for the larger cobalt area, the radium, and smaller cobalt area. The small cobalt area and radium area are suitable for comparison of erythema: same doses, no previous roentgen therapy, located similarly to the large area of external irradiation and interstitial implantation.

The reactions over the cobalt and radium areas differed in two ways: (1) Over the radium area a faint, fast subsiding erythema was present, with bands of brisker erythema over the needles; this shows the lack of uniformity of dosage to sensitive layers. A brisk erythema developed over the cobalt within a week, evolving into partial moist desquamation which healed in four weeks. (2) The holes of entry of the radium needles did not show (as is the case if the needle ends have been well buried) evidence of acute slough and healed rapidly. This was true even for the crossing radium needles implanted at the margin of the internal mammary chain field. On the other hand, large sloughs (up to 0.75 cm. in diameter) developed around the holes of entry of the cobalt needles (*C*). They were not healed at four weeks.

In order to eliminate individual variations in skin sensitivity, the best approach is to perform implants partly with radium and partly cobalt needles in the same area of the body of a patient. Chest wall implants for carcinoma of the breast are large enough so that the sub-areas are sufficiently independent from the contribution of the other areas to develop their own characteristic skin reactions.

A first implant was performed on a post-mastectomy case (Fig. 8) using partly cobalt and partly radium needles. The doses are those delivered to the 0.5 cm. plane and are not the actual doses to the sensitive structures of the skin (1 to 3 mm. below the surface[15]). A strong suggestion of the correctness of this hypothesis is the fact that over the radium implant the reaction was stripe-like with brisker erythema over the needles and barely perceptible erythema in between. One would not expect such

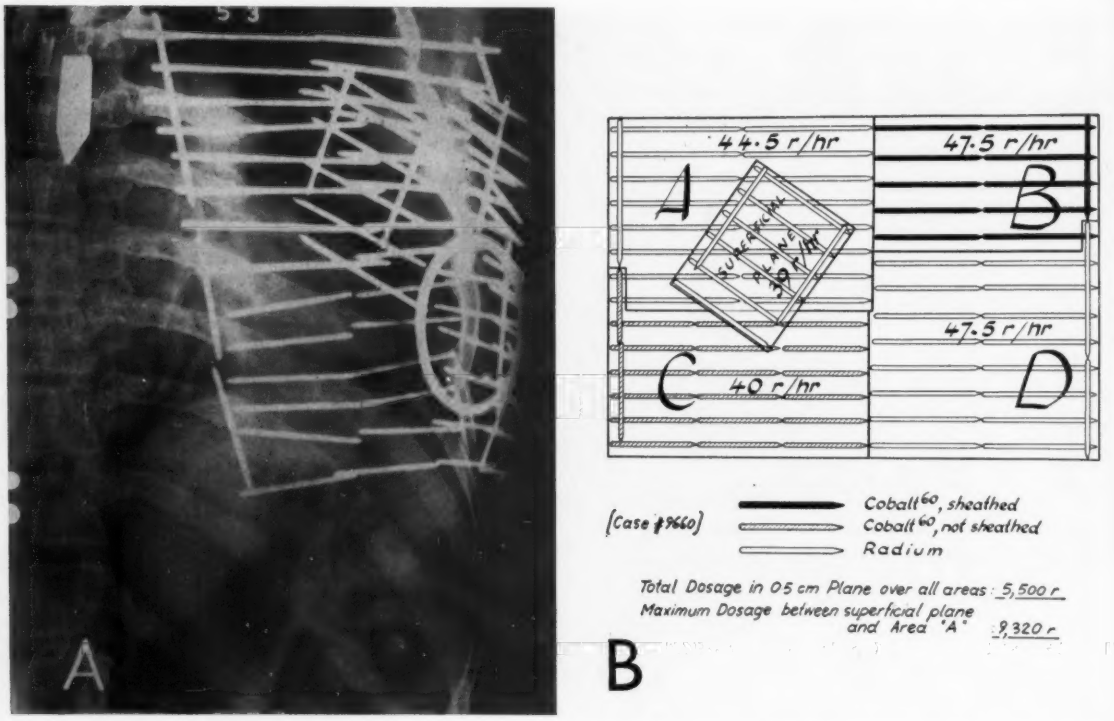


FIG. 9. (*A*) Roentgenogram. (*B*) Diagram of needles. (*C*) Color print five days after removal of needles. (*D*) Color print two weeks after removal of needles. It can be seen that the greatest reaction remained in the commercial cobalt implant, both skin reaction being greater and necrosis being near sites of entry of needles. The skin reaction with unsheathed cobalt was slightly greater than that of the radium but no necrosis occurred around the sites of entry.

Fixed, inoperable carcinoma in a small breast. The chest wall was implanted with a large planar implant reinforced by a superficial plane in the breast itself. The large implant was made of four parts (*B*). The dosage rates in the various areas were carefully computed and the needles were removed at different times in order to deliver 5,500 gamma roentgens to the large planar implant. The areas B, C, and D are suitable for comparison.

A stripe-like erythema developed over the radium area (area D) in contradistinction to a uniform, brisker erythema over the cobalt areas (areas B and C). In addition, the erythema along the lateral border of B and C extended outward in a fading away fashion while it was limited and sharply defined by the peripheral needles of the radium implant. Moist desquamation was generalized over B, C, and D but epithelization started earlier and progressed faster over area D. Acute slough developed at the holes of entry of the unsheathed needles (area C). The holes of entry of radium needles and sheathed cobalt needles showed no evidence of radiation slough.

a difference in the plane of calculation because the uniformity of dosage is within 10 per cent of the average dose.

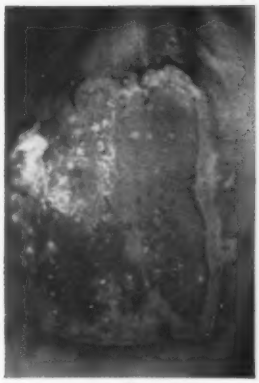
A brisk, uniform erythema developed over the cobalt area, evolving into moist desquamation almost over the whole area. This uniformity of reaction is not in conflict with the statement made above. It means that the minimum dose between needles was sufficient to produce maximum skin erythema. It happened that over the radium area the variations of doses were over the range producing degrees of intensity of erythema.

More striking was the difference at the holes of entry of the cobalt and radium needles. The radium needle holes exhibited only evidence of mechanical trauma, healed completely in two weeks. This is usual, if the eyelets have been well buried as they ought to be in a carefully done implant. In contradistinction, within a week after

8C

8D

9C



9D

removal of the needles, large acute sloughs (up to 0.75 cm. in diameter) developed around the cobalt needle holes and were still unhealed four weeks later.

A second implant was then performed using partly radium and partly commercial cobalt needles and secondary sheathed cobalt needles in order to investigate general skin reactions and hole damage. The erythema, moist desquamation, and epithelization ran a similar course both in intensity and time over sheathed and unsheathed cobalt needles. Over the radium area again a stripe-like erythema was seen: bands of brisker erythema developed over the needles. The moist desquamation was complete over the radium area but healed faster than over either cobalt area. The reaction was sharply delineated at the margins of the radium area, extending over the peripheral skin of the cobalt areas in a more fading-away fashion. Radiation sloughs developed only at the holes of entry of the unsheathed cobalt needles, showing that the longer dead ends of the sheathed needles had reduced adequately the excessive doses.

In these two subcutaneous implants, for the same "average tumor dose," the general skin reactions (erythema, moist desquamation and healing time) were more severe over the cobalt areas (commercial and extra sheathed) than over the radium area. This is easily accounted for by the higher dose ratio in the vicinity of the plane of the needles and around the needles. The radiation slough at the holes of entry of the commercial needles was excessive and was eliminated by the addition of a sheath with longer dead ends so that the end of the active cobalt wire is no longer flush with the skin structures at the hole.

Greater severity of mucositis and larger sloughing areas ought to be expected in submucous implants because, due to the lesser thickness of the mucous membranes, the sensitive layers are in contact with the surface of the needles and the ends cannot be as deeply buried. Severe "hole effects" will also be present in straight tongue implants as the eyelet is flush with the surface in order to suture the needles firmly.

CONCLUSION

(1) A more unfavorable (damage/tumor control) ratio may exist in cobalt interstitial therapy with either needles or nylon threads than with radium needles. Great caution should be exercised before replacing well established radium techniques of using needles heavily filtered with platinum in curable lesions of the skin and oral cavity where a long survival is expected and where late damage (greater atrophy or even necrosis) is of paramount importance both cosmetically and functionally.

(2) Small diameter needles produce more acute radiation slough around the needles due to higher surface doses. The mucous membrane and skin damage at the holes of insertion is excessive and longer dead ends ought to be used to minimize the effect. This unnecessary damage which causes increased discomfort, delayed healing, atrophy and late complications can be minimized by thicker needles (at least 14-gauge for 3 cm. active length and up) and longer dead ends. It would appear desirable to design cobalt needles such that the surface dose rates are of the same order as those which have been found to be tolerable in radium practice. A suggested design would be 0.5 mm. cobalt 60 wire in 14-gauge steel, with 5 mm. dead ends.

(3) Cobalt sources can be used to good advantage in intracavitary therapy. Extra sheaths with tungsten screening at both ends should be used for protection of bladder and rectum in the vaginal applicators employed for cancer of the cervix. Similarly, a tungsten plug should be placed at the end of the uterine tandem.

(4) Tables of linear sources can be used with a conversion factor based on the relative dose rates at a distance. Similarly, the Paterson-Parker system can be used with the same conversion factor as the 5 per cent higher "average dose" is well

within the accepted limits of physical variations.

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DISCUSSION

DR. JOSEPH L. MORTON, Columbus, Ohio. It is with much pleasure that I discuss this most excellent paper of Dr. Fletcher and his group. This is a work well done. It would appear that the cobalt needle as found by them commercially will require some modification either in design or use before it will meet clinical standards and can be substituted for weak radium needles. This finding we believe to be due to two factors—the inherent needle construction along the lines of a radium needle and the inherent lack of self filtration of the cobalt metal as compared with the dense radium salt. The recommendations Dr. Fletcher makes are essentially worth while if one is going to insist that cobalt resemble radium in every detail, namely to increase the sheath diameter and to increase the end filtration.

Before committing ourselves to this handcuffing of a new material to an old technique I would recommend a re-examination of the basic principles of the Paterson and Parker system as I understand them, namely that the system be considered an approximation valid to within 10 per cent for a distribution of finite sources of irradiating material to give a uniform distribution of radiation in a plane or volume not closer than one-half the space between sources. This is a geometrical function made possible by the assumption that the diminution due to absorption in tissue is equal to or approximates the increment due to scatter as measured in roentgens if the gamma-ray energy is over 600,000 volts.

Considering the problem from this viewpoint, there is no preference for needles and the simplest approach is to choose point sources or a reasonable approximation of the same. To us the usefulness of the Paterson and Parker tables is as a method of beginning to approximate the arrangement needed to reproduce a uniform pattern. This gives a starting arrangement clinically usable which is then converted

to some linear arrangement. Irradiation by points, lines or planes is unimportant provided one can get a uniform pattern. The manufacturers of radium needles employ the spacing technique to approximate heavy end loading and diminish the central buildup from a large continuous source. This was possibly accidental originally in order to prevent the powder from accumulating in one end of the needle. At least I have not found the original theoretical discussion of the principles of needle loading in the radium literature. Practically speaking, the insertion of needles is easier than either of the other methods unless the area is amenable to a plaque.

The choice of a number of small relatively hot points rather than a continuous line of interstitial sources would appear to be biologically advantageous. Adjacent to the source there is always an overdose. This so-termed "periacicular necrosis" of the Melbourne school led them to filter radon and radium with 0.8 mm. of gold to avoid the estimated 5 per cent of beta emission through 0.5 mm. of gold or platinum, as well as the near distance, inverse square law type of effect. If the source is uniform along the axis, as thin walled and as large in diameter as was the commercial needle of Dr. Fletcher, there is a summation of this radiation into a cylinder along the needle axis. If the sources are more nearly points as we find easiest to use and calculate (0.5 by 3 mm. cylinders) there is an area along the needle tract which is not over-irradiated and the damaged tissue represents a series of spheres. Everyone is familiar with the improved tolerance of tissue when the overdosage is in smaller units as witness the Hirsch Marks grid. As to mechanical injury, it must be less with the smaller cross section of a needle 1.25 mm. in diameter which has two and a half times less cross sectional area than a 2 mm. needle. One can feel the difference in the ease with which they are inserted. Therefore, the two components of "periacicular necrosis" the mechanical pressure trauma and the spot necrosis from overdosage of radiation favors the use of point sources rather than solid linear sources. Initial animal experiments indicated this to us when we were unable to find the needle tracts either microscopically or grossly with 10,000 r given with small point source type of needle loading pattern.

Regarding Dr. Fletcher's objection to the dosage outside the volume implanted, this he admits is greatest in the small implants and becomes less significant as the implant reaches larger size. This is to us no objection but an advantage to be cherished. One who has not had the error of mistakenly treating too small an area only to see the tumor recur outside the effective dosage range, to his sorrow, either has the wisdom of Solomon or does not follow up his cases. It is with the small lesion that this error is the most tragic for here exists the best possible chance for cure. Conversely, it is the small lesion where the danger from total body tolerance is the least for the total volume treated is likely to be insignificant so that an increase is tolerable in the dose outside the treated area. The ability to irradiate a millimeter or more effectively into bone should not be overlooked for the insertion of needles is here more difficult and less likely of reaching a successful pattern.

In summary, we find Dr. Fletcher's facts valid, his warnings well taken and his paper timely and appropriate. However, that this is the final answer to the choice between cobalt and radium we doubt.

PERCUTANEOUS ABSORPTION OF TRITIUM OXIDE*

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TRITIUM, the mass 3 radioactive isotope of hydrogen, promises to become a widely used tracer for hydrogen in biological and chemical studies. Hazards attendant on the handling of this isotope are limited to those from internal radiation, the energy of its beta particle being so weak (maximum energy, 0.0185 mev.) as to constitute no external radiation hazard. In part, then, the problem of hazard evaluation becomes one of studying the various portals through which tritium, or compounds containing tritium, may gain entry to the body. The present paper is concerned with the hazards arising from a tritium oxide contaminated atmosphere.

The two main portals through which atmospheric tritium oxide may enter the body are presumed to be the lungs and the skin. The contribution of pulmonary absorption to the total body uptake from an atmosphere of known tritium oxide content can be readily calculated on the assumption that all tritium oxide entering the lungs is absorbed. This assumption has been experimentally verified by several investigators.[7,12,19] The contribution from absorption through the skin must be measured experimentally. The present investigation was made to determine the rate of percutaneous absorption of tritium oxide, to compare this with the rate of pulmonary absorption, and to investigate the factors which might be important in determining or changing the rate of absorption. While principal attention was focused on absorption from the vapor state, experiments were also performed to compare the rate of absorption of liquid water.

To the extent to which tritium may be considered a legitimate tracer for hydrogen, the results of this study contribute to the general problem of the permeability of the skin to water. Positive proof of the inward passage of liquid water has only recently been reported.[22] A preliminary note on our demonstration of the percutaneous absorption of water vapor has appeared in the literature,[9] and a recent review by Pinson[18] alludes to unpublished studies on percutaneous absorption of tritium oxide performed at the Los Alamos Scientific Laboratory.

METHODS

Subjects and Exposure Procedures. Subjects employed were CF-1 strain mice, rats of the Sprague-Dawley strain, and human, adult, white males. Except for a single total body exposure of a human subject, all exposures were to a circumscribed skin area. Unless otherwise specified, exposures were for one hour at 30° C. Animals were exposed under nembutal anesthesia.

Two systems were employed for exposure of the skin to the tritium oxide-labeled water vapor. The first of these, illustrated in Figure 1, consisted of a small cup containing tritium oxide in water* supported above the skin inside of a containing chamber. This apparatus will be subsequently referred to as the "static" system. Because of inadequate saturation of the air in the system and because of the danger of spilling liquid tritium oxide solution on the skin, a second type of apparatus, illustrated in Figure 2, was employed for the major portion of the investigation. This "dynamic" system consisted of a hydrator into which dried air was passed, via a sintered glass gas dispersion tube, through a water solution of tritium oxide and thence into a connected exposure chamber in which the saturated vapor was passed over the skin and out into a dry ice trap. Control experiments

* It will be recognized that the proportion of tritium oxide in the water solutions was, masswise, extremely small, and that the molecular species present which contained tritium was almost exclusively HTO.

* This paper is based on work performed under Contract No. W-31-109-Eng-52 for the Atomic Energy Commission.
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demonstrated that saturation in the dynamic system was maintained at 96 per cent of the theoretical values. In certain of the experiments in which the effect of vapor pressure was to be studied, the solution in the hydrating vessel contained varying proportions of dissolved sodium hydroxide.

The exposure chambers were held against the skin area by application of slight pressure. The juncture was sealed with collodion in early experiments, but this precaution was found to be unnecessary.

Areas exposed were as follows: human subjects, 9.8 cm.^{2} either on volar surface of forearm or on abdomen; rats, 6.6 cm.^{2} on abdomen; mice, 2.8 cm.^{2} on abdomen. The areas to be exposed on rats and mice were shaved a day prior to exposure, and any animal whose skin was nicked in the process was discarded. Exposed areas on human subjects were not shaved.

The total body exposure experiment was conducted in a gas-tight chamber approximately 4 feet on a side. Uncontaminated respiratory air was supplied under slight pressure through a nosepiece and mouthpiece. A continuous stream of tritium oxide-labeled water vapor was passed into the chamber at a rate of approximately 5 liters per minute. Exit air was passed through a large ionization chamber connected to a recording micro-microammeter. Because of the large volume of the exposure chamber it was impossible to maintain exactly constant conditions throughout the fifty-two minute exposure period. The concentration of tritium oxide in the chamber atmosphere varied from 3.7–4.8 μc/liter with a weighted average of 4.2 μc/liter. Temperature of the air averaged 30° C. and the relative humidity averaged 70 per cent.

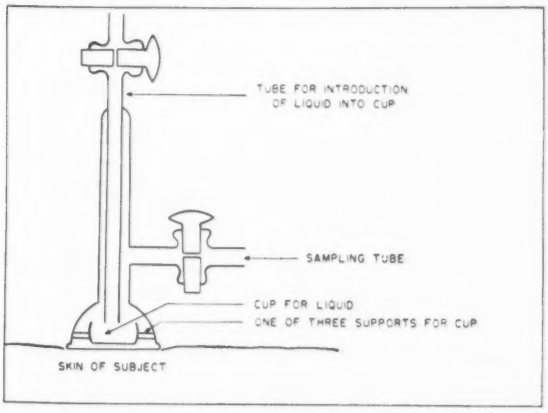

Fig. 1. "Static" skin exposure apparatus.

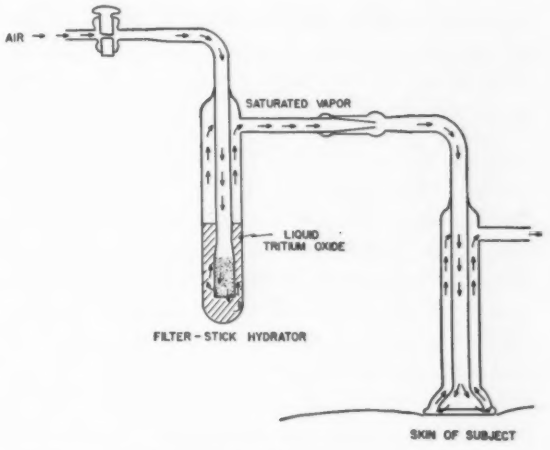

Fig. 2. "Dynamic" skin exposure apparatus.

The subject was unclothed except for loose-fitting shorts, and was perspiring freely during most of the exposure period.

Rats were exposed to liquid physiological saline containing tritium oxide by placing a 2 cm. layer of the liquid confined in the female end of a hemispherical glass joint over the skin area. Solutions employed were warmed to 30° C. before application. Following exposure, the liquid was carefully removed, the exposed area washed with detergent, thoroughly flushed under a tap, and then dried.

Sampling and Counting. Tritium oxide absorption was measured by analyzing samples of body water obtained by several different methods. Rats and mice were sacrificed following exposure, the carcasses ground, and total body water separated by azeotropic distillation with benzene. In the case of rats a cardiac blood sample was also taken immediately following exposure and analyzed as an indication of the rapidity with which absorbed tritium oxide is distributed in the body water. Sampling of human subjects was confined to a series of urine samples taken over a forty-eight hour period following exposure. The peak urine activity, attained several hours following exposure, was used in calculations.

Counting of the samples for tritium activity was accomplished by one or both of the following methods: (a) generation of hydrogen gas by addition of the water, blood serum, or urine sample to calcium metal and counting of the gas in a G. M. tube filled to atmospheric pressure and externally quenched; (b) addition of the sample to calcium carbide for conversion to

acetylene, which gas was then introduced into an ionization chamber connected to a vibrating reed electrometer. The current produced was measured as a function of the length of time required to discharge a standard negative potential. Currently the hydrogen-filled Geiger counter has supplanted the vibrating reed electrometer because of ease and rapidity of operation and maintenance. Results obtained by either of these methods are reproducible with ±5 per cent. Absolute values may be subject to greater error due to uncertainties in the absolute calibration of the instruments and possibilities of slight isotopic fractionation in the generation of gas samples. Such absolute errors are not of significance in the present study, since all conclusions are based on comparisons of counts. Details of the counting procedure will be described by others.[10]

Expression of Results. Results are expressed in two forms. An absorption rate constant, K, is in units of μc tritium oxide absorbed per cm.² skin area per minute per μc/cc. of tritium oxide in the exposure atmosphere. In terms of experimentally determined quantities, this constant is calculated in the following manner:

$$K = \frac{UC_i}{AtC_e}$$

where U is the total volume of body water (liters), C_i is the activity of the body water (μc/liter), A is the area exposed (cm.²), t is the duration of exposure (minutes), and C_e is the activity of the exposure atmosphere (μc/cc.).

Results are also expressed as the quantity of water absorbed (in μg.) per minute per cm.² skin area. The symbol Δ is employed for this quantity which is calculated in the following manner:

$$\Delta = \frac{UC_i}{AtS}$$

where S is the concentration of tritium in the water employed, in μc/μg. This calculation, of course, assumes that tritium oxide functions as an ideal tracer for water, both in biological absorption and in the physical evaporation to form the saturated atmosphere. While this assumption cannot be strictly valid, error introduced by the assumption is no doubt smaller than other errors inherent in this type of study.

The values for total volume of body water were experimentally determined in the case of the rats and mice, and estimated at 61.8 per cent of total body weight in the case of the human subjects.[20]

The plus-or-minus limits listed with values of K and Δ are standard deviations of the mean at the 95 per cent confidence level.

RESULTS AND DISCUSSION

The results obtained from exposure of the various species to a saturated or near saturated water vapor atmosphere are recorded in Table I. Data for male and female rats and mice were calculated separately, but no sex difference was apparent and the results for both sexes were combined. The results obtained using the static exposure

TABLE I

PERCUTANEOUS ABSORPTION OF TRITIUM OXIDE FROM A SATURATED OR NEAR SATURATED WATER VAPOR ATMOSPHERE AT 30° C.

Subject	Method of Exposure	Site of Exposure	Pre-exposure Treatment	No. of Subjects Exposed	Absorption Rate Constant for Tritium Oxide = K (μc/cm.²/min./μc/cc.)		Water absorption rate = Δ (μg./cm.²/min.)	
					Based on cardiac blood sample	Based on sample of total body water	Based on cardiac blood sample	Based on sample of total body water
Rat	Static	Abdomen	Unshaved	21	.018 ± .003	.055 ± .010	.55 ± .07	1.67 ± .31
Rat	Static	Abdomen	Shaved	25	.082 ± .017	.141 ± .026	2.29 ± .45	4.06 ± .54
Rat	Dynamic	Abdomen	Cloth covering (shaved)	24	.175 ± .029	.189 ± .035	5.31 ± .87	5.70 ± 1.06
Rat	Dynamic	Abdomen	Shaved	30	.134 ± .015	.188 ± .018	4.06 ± .46	5.70 ± .53
Mouse	Dynamic	Abdomen	Shaved	29	—	.67 ± .16	—	20 ± 5
Man	Dynamic	Forearm	Unshaved	12	—	.28 ± .05	—	8.6 ± 1.7
Man	Static	Abdomen	Unshaved	2	—	.34	—	10.4
Man	Dynamic	Total body	Unshaved	1	—	.84	—	17.8

system are low to an uncertain degree for reasons previously discussed. They are included in Table I only for purposes of qualitative comparison. It should be noted that data published previously in a preliminary note[9] were obtained by the static method and are therefore not in agreement with the best values here reported. The "static" data from rats included in Table I do indicate quite clearly the enhanced absorption occasioned by shaving the exposed area.

In all cases the values of K and Δ calculated from cardiac blood samples are lower than the corresponding values calculated from samples of the total body water, indicating a lag in the distribution of the absorbed water. This effect was noted and studied more extensively with short-term exposures by Pinson.[18] With respect to the eventual body burden, however, the values based on samples of total body water are of primary significance, since uniform distribution of the absorbed activity must certainly occur within a period of time which is short compared with the biological half-life of tritium oxide in the body.

The experiment in which a series of rats were exposed with a layer of cloth covering the skin area was designed to evaluate possible effects of clothing on percutaneous absorption. The cloth employed was heavy cotton material of the type commonly found in laboratory coats and coveralls. No effect was observed on total absorption, as indicated by the K values calculated from total body water samples. There does appear to be an increase in the rate at which the absorbed activity appears in the circulation as evidenced by the values of K calculated from the cardiac blood samples.

The data from human subjects are characterized by a lack of agreement between the results obtained for different exposure sites. The agreement between the data from 12 subjects exposed on the forearm was quite good, considering the disparity in physiques and the consequent error in assuming a constant proportion of body water in all subjects. While the two exposures to the abdomen were made using the static system, the results are of qualitative interest, since they indicate a higher rate constant for the abdomen than for the forearm. The quantitative difference is undoubtedly greater than that indicated, since all of the data obtained with the static system were low compared with results obtained using the dynamic system.

The single total body exposure experiment indicates an absorption rate constant about three times as great as the constants calculated from forearm exposures. Several factors must be considered in evaluating this result. First, it is obviously unsafe to generalize too extensively from the results of a single exposure. Second, the conditions of this total body exposure were somewhat different from those which existed in the forearm exposures. While the forearm exposures were performed in an essentially saturated water vapor atmosphere, the average per cent saturation during the total body exposure was only 70 per cent. This difference, while influencing Δ values, should not affect K values, as will be shown in later discussion. Third, the subject involved in the total body exposure was one of the subjects included in the forearm exposure group, the K value from his forearm exposure being 0.23, thus strengthening the evidence for a real difference in absorption rate between different skin areas.

Pinson[18] has suggested that percutaneous absorption of water vapor could be looked upon simply as the reverse phase of the physiological phenomenon of insensible perspiration. If this is the case, and it appears entirely reasonable, then the extensive data previously collected on insensible perspiration should be pertinent to an understanding of percutaneous absorption. Table II lists some of the results obtained over the past thirty-five years, recalculated where necessary to a common basis of μg. water loss per cm.^{2} per minute. Where original data were given in terms of the total body surface an average skin area of 1.8 M^2 was assumed, and it was further

TABLE II

INSENSIBLE WATER LOSS THROUGH THE SKIN
LITERATURE VALUES

Portion of Body	State of Skin	Rate of Loss (μg./cm.^{2}/min.)	Environment	Reference	Year
Total body	Living	13	—	(21)	1917
Total body	Living	25–30	—	(15)	1931
Total body	Living	25	Liquid, 72° F.	(23)	1932
Index finger tip	Living	120	75° F.	(14)	1941
2nd toe tip	Living	79	50% rel. hum.		
Pinna	Living	32			
Leg	Living	15–20	28° C.	(17)	1942
Ball of foot	Living	180	75° F.	(3)	1943
Plantar surface, heel	Living	160	50% rel. hum.		
Palm	Living	150			
Index finger tip	Living	150			
Lateral surface, arm	Living	140			
Mid plantar, foot	Living	120			
2nd toe tip	Living	88			
Cheek	Living	71			
Mid forehead	Living	70			
Axilla	Living	62			
Posterior surface, leg	Living	53			
Thigh and flank	Living	41			
Mid epigastrium	Living	37			
Volar surface forearm	Living	29			
Epigastrium	Living and dead	100*	75° F.	(24)	1944
Epigastrium	Living and dead	100*	75° F.	(4)	1944
Total body	Living	16	75° F.	(5)	1945
Total body	Dead	9	50% rel. hum.		
Palm	Dead	29	24° C.	(6)	1946
Sole	Dead	18	70% rel. hum.		
Axilla	Dead	10			
Epigastrium	Dead	3.3			
Total body	Living	13	23° C. 51% rel. hum.	(8)	1948
Palm	Living	70–150	27° C.	(16)	1951
Sole	Living	50			
Face	Living	40			
Arm, leg and trunk	Living	7			

* These studies indicate a maximum rate, since dried O_2 was passed over the skin.

assumed that 52 per cent of the total insensible water loss was via the lungs.[5] These figures represent net water loss and constitute the balance between the outward and inward movement of water through the skin. As such, they bear no necessary relationship to the magnitude of either of these individual processes. If, however, the

TABLE III

EFFECT OF WATER VAPOR PRESSURE ON PERCUTANEOUS ABSORPTION OF TRITIUM OXIDE

Expt. No.	NaOH Molarity	Theoretical		Experimental		No. of rats exposed	K (μc/cm.^{3}/min./μc/cc.)	Δ (μg./cm.^{2}/min.)
		Vapor pressure (mm. Hg)	Conc. of $T=C_e$ (μc/cc.)	Vapor Pressure (mm. Hg)	Conc. of $T=C_e$ (μc/cc.)			
1	0	31.8	7.57	30.5	7.28	30	.188 ± .018	5.70 ± .53
2	8	19.4	4.44	20.3	4.65	11	.186 ± .033	3.30 ± .59
3	13	10.7	2.39	10.5	2.34	11	.158 ± .044	1.51 ± .42
4	16	7.2	1.58	7.47	1.64	11	.199 ± .032	1.26 ± .20
5	18	5.0	1.09	5.85	1.31	10	.135 ± .024	.705 ± .124
6	29.4	0.9	0.18	1.73	0.347	11	.245 ± .048	.340 ± .067

mechanism of inward and outward passage of water through the skin is identical or closely similar, one would expect that high net water movement would be associated with high rates of movement in both directions. It is evident from an inspection of the data of Table II that the rate of net water loss varies considerably in different skin areas. The one series of studies which included the volar surface of the forearm shows a lower rate for this area than for any other area measured. It thus appears not unreasonable that the average total body rate of percutaneous absorption should exceed the forearm rate by several fold; and, although based on a single determination, the value of 0.84 μc/cm^2/min /μc/cm.^{3} atmosphere is probably a reasonably accurate measure of the total body percutaneous absorption rate constant.

Data on the effect of water vapor pressure on the percutaneous absorption of tritium oxide in rats are summarized in Table III. These experiments were conducted in a manner exactly similar to the other exposures, except that the water vapor pressure in the exposure atmosphere was controlled by addition of sodium hydroxide in various concentrations to the tritium oxide solution in the hydrating chamber of the "dynamic" exposure apparatus. Table III lists both the calculated vapor pressure and tritium concentration of the atmosphere[1,13] and their values as determined experimentally by sampling the atmosphere. Satisfactory agreement was obtained, except for the two highest sodium hydroxide concentrations. In these two cases the theoretical values were based on extrapolation, and the experimental figures are undoubtedly the more accurate of the two. In calculating values of K, theoretical C_e values were used for experiments 1–4 and experimental values for experiments 5 and 6. Values of K and Δ in Table III were based on tritium determinations on the total body water from the exposed animals. Blood samples were also analyzed and led to values of K and Δ which were consistently about 70 per cent of the total body water values, indicating again a time lag in the equilibration of absorbed tritium oxide with the total body water.

It is evident from Table III that the rate of water absorption (Δ) is directly proportional to water vapor pressure. It is also clear that the absorption of tritium oxide from an atmosphere of constant tritium oxide content (K) is independent of total water vapor pressure. The direct proportionality between water absorption and water vapor pressure supports the hypothesis of a simple diffusion mechanism for percutaneous absorption. From the hazard standpoint, the results indicate that humidity is not a factor to be considered in exposure considerations.

The results of liquid water absorption studies on the rat are shown in Table IV. Absorption rates were calculated from analyses on total body water. The much higher values obtained from unshaved animals must be attributed to tritium-labeled

TABLE IV

PERCUTANEOUS ABSORPTION OF LIQUID WATER BY THE RAT

Expt. No.	No. of Rats	Auxiliary Treatment	(μg./cm.^{2}/min.)
1	17	Shaved prior to exposure	15.2$\pm$3.0
2	5	Unshaved	31.3$\pm$4.7
3	5	Shaved subsequent to exposure	10.6$\pm$3.5

water adsorbed on the hair and included in the total body water determinations. Shaving either before or after exposure reduced the values. The results of experiments 1 and 3 are not significantly different considering the small number of animals in experiment 3. The absorption rate appears to be two to three times larger for liquid water than for saturated water vapor. These results on liquid water should be considered only as preliminary findings; and the possibility of extensive adsorption on the skin, resistant to thorough washing, should not be overlooked. So far as the eventual body burden is concerned, however, any such tightly adsorbed water is practically equivalent to absorption. Pinson[18] has reported no difference in the absorption rate from liquid water or a saturated water vapor atmosphere.

RELATIVE HAZARDS OF PERCUTANEOUS VERSUS PULMONARY ABSORPTION OF TRITIUM OXIDE VAPOR

Using the value of 0.84 for the absorption rate constant for human total body exposure (Table 1), a "standard man"[11] during an eight hour period of exposure to the presently established permissible maximum[11] will absorb 360 μc through his skin:

Absorption rate constant (0.84) $\times$ total skin area (1.8×10^4cm.^{2})* $\times$ time (480 min.) $\times$ tritium oxide concentration in atmosphere (5×10^{-5} μc/cc.) = 360 μc.

* This represents the total skin area of a 70 kg. and 170 cm. man.[2]

Similarly, for pulmonary absorption, assuming complete retention of inhaled tritium oxide, a value of 500 μc is obtained:

Volume inspired (10^7cc.) $\times$ tritium oxide concentration in atmosphere (5×10^{-5} μc/cc.) = 500 μc.

From these calculations it is apparent that percutaneous absorption and pulmonary absorption contribute approximately equally to the total body burden of tritium oxide acquired through exposure to an atmosphere contaminated with tritium oxide.

The present permissible maximum level for atmospheric tritium oxide contamination was established without consideration of percutaneous absorption. A reduction in the permissible maximum by a factor of two is therefore suggested by the results of the present investigation. The establishment of percutaneous absorption as a significant hazard also emphasizes the inadequacy of respiratory protection alone in tritium oxide contaminated atmospheres.

SUMMARY

The percutaneous absorption of tritium oxide-labeled water vapor was studied in mice, rats and man. In terms of μg. water absorbed/cm.^{2}/min. from a saturated water vapor atmosphere, the rates found were: for mice (abdomen), 20$\pm$5; rats (abdomen) 5.7$\pm$1.1; man (forearm) 8.6$\pm$1.7. A single total body exposure to a human at 70 per cent relative humidity gave a rate of 18 μg/cm^2/min. The rate of water vapor absorption in the rat was found to be directly proportional to water vapor pressure. For a constant level of atmospheric tritium oxide, absorption of tritium oxide was independent of total water vapor pressure.

It was shown that for humans the rate of percutaneous absorption of tritium from a tritium oxide contaminated atmosphere is about the same as the rate of pulmonary absorption from the same atmosphere.

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EXTRAPOLATION IONIZATION CHAMBER FOR MEASUREMENT OF DOSAGE IN INTRA-CAVITARY IRRADIATION*

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IN 1948 experiments were begun with small cylindrical sources of Sr^{90} and $Ru\text{-}Rh^{106}$ for intragastric irradiation in dogs. The sources were mounted at the end of a wire with retractable shields. A thin rubber balloon enclosed each unit so that, upon inflation with air to a volume of 525 cc., the isotope would be at the center of a sphere approximately 5 cm. in radius. The design was planned to insure fairly uniform irradiation of the acid-secreting regions of the stomach in the dog.

$Ru\text{-}Rh^{106}$ was electroplated on the surface of a brass cylinder 1.8 mm. long and 6 mm. in diameter by the Oak Ridge Laboratories. A very thin layer of silver was then plated over the surface of the isotope to prevent loss of the active material upon accidental exposure to acid gastric juice.

The amount of radioactive material used was based on the finding of Ricketts, Palmer *et al.*[6] in man that the optimal dose with 200 kv. (peak) roentgen rays (half-value layer, 1.5 mm. Cu; filters 1 mm. Cu+1 mm. Al, 33 r/min., 50 cm. focus skin distance, one anterior and one posterior portal) for the treatment of peptic ulcer was 1,600 roentgens. Accordingly, Mr. L. D. Marinelli of Argonne National Laboratories, advised the use of 125 mc. to obtain a reasonable treatment time. The output of our source was measured at the Oak Ridge Laboratories before shipment and was estimated to be approximately 6,000 r/hr. at 2.5 cm.

Accurate measurement of dose was necessary not only for experimental purposes, but because it was intended to consider use of this instrument in man, if its feasibility could be established in the dog.

Because of the unusual geometric design, filtration by the silver plating and the rubber balloon, and scattering and formation of roentgen rays in the heavy metal base, an instrument was designed by one of us (A.L.) for measurement of surface dose under conditions approximating those of actual use. With Failla's original design[3] as a basis, modifications were employed as suggested by instruments made by Krohmer and McCarthy[4] and Tracerlab, Inc.[7] with the advice of Dr. R. K. Clark of the Argonne National Laboratory.

To fit the circumstances of intracavitary use, a spherical plexiglass phantom was constructed. When the irradiating unit is suspended in its center, the physical factors of actual use are simulated, as shown in Figure 1.

There is an opening at the bottom of the sphere through which the radiation enters the lower chamber. The lower portion consists of a brass cup with a polystyrene insulator disc at its base. Thin rubber dam is stretched tightly over the flat bottom surface of the plexiglass phantom. A thin aquadag coating is applied to the lower surface of the rubber dam, making contact with brass electrodes connected to batteries. Thus the rubber diaphragm serves simultaneously as an absorber in the path of the radiation, as in use, and as the upper plate of the ionization chamber.

The surface of the polystyrene disc in the bottom of the brass cup is also coated thinly with aquadag. In the center of

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the disc a circle 1.5 cm. in diameter is scribed to isolate the current collecting area. A graphite electrode passes out from the center of the collecting area through a cylindrical polystyrene insulator. This graphite conductor leads to a coaxial connector which is connected with a rigid coaxial cable to a Beckman micro-micro-ammeter. The surface of the polystyrene disc outside the collecting circle and the brass cup are grounded.

The upper section of the assembly is threaded to fit into the brass cup so that the distance between upper and lower plates may be varied by turning the upper part. The upper piece is provided with a pointer which moves over a scale scribed on the outer surface of the brass cup. Thus an accurate measurement of plate separation distance is provided. This measurement is obtained by rotating the upper section in the cup until electrical contact is made. The reading on the scale is recorded and the upper section is then rotated upward and a series of readings obtained at various plate separation distances. These data are plotted on a graph (Fig. 2) with ionization current as a function of plate separation.

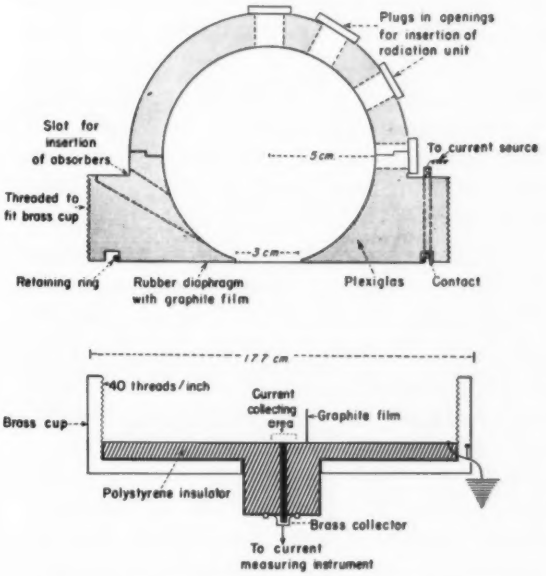

Fig. 1. Extrapolation chamber with spherical phantom to simulate intracavitary use.

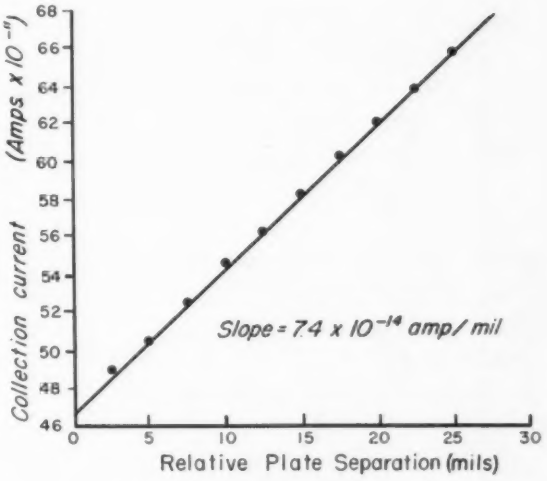

Fig. 2. Ionization current at various plate separation distances.

The volumetric rate of charge collection (R) can readily be calculated from the slope of the line (u amps/mils) when the area of the collection plate and suitable constants are included. A convenient formula is that of Brinkerhoff:[1]

$$R = 1.83 \times 10^{11} \cdot \frac{m}{A} \cdot \frac{760}{p} \cdot \frac{273+t}{273} \cdot \frac{\text{esu}}{\text{cm.}^3} \text{ sec.}$$

Where m is the slope in u amps/mil; A is the collection area in sq. mils, p is the atmospheric pressure in mm. Hg, t is the room temperature, °C.

The result is the surface dose in esu/cm.^{3}-sec. at S.T.P., which is approximately equivalent to the rep/sec. The dose produced on the collecting surface of the 5 cm. radius sphere by our source in a horizontal (0°) position was 0.0605 esu/cm.^{3}-sec or 217.8 esu/cm.^{3}-hr. The activity of the source, corrected for decay, was 27.5 millicuries, based on the estimate of the original activity at Oak Ridge. Hence the surface dose can be expressed as 7.9 esu/cm.^{3}-mc.-hr. at a point 5 cm. from the center and equidistant from the ends of the source.

Absorption Curve. Lucite discs 3 cm. in diameter and of various thicknesses were placed over the diaphragm, resting on the base of the phantom. For each thickness a

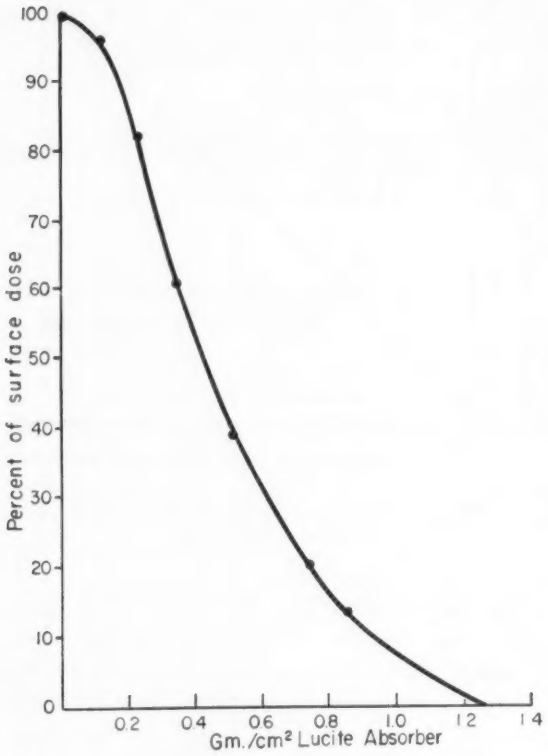

FIG. 3. Per cent reduction of surface dose with various thicknesses of lucite.

new set of data were taken and graphed to determine the slope. The resulting percentage of maximum dose was plotted as a function of the thickness of the lucite absorber in gm./cm.^{2}. This curve is shown in Figure 3 and is in good agreement with one determined by Cara[2] using a photographic method with a plaque source of Ru-Rh^{106} 1.5 cm. in diameter at a 10 cm. distance.

Radiation Pattern. Measurements were made with the applicator at 30° and at 60° to the horizontal. At 30° the intensity had not appreciably decreased, while at 60° it had decreased to 51 per cent.

This variation of intensity is due to geometrical factors, self-absorption within the unit and in the brass disc at the cylinder end, and differs from the angle intensity variation for linear gamma-ray sources.[5] Measurements with the source in the vertical position were attempted but could not be made because the ionization current was too small to be measured with our instruments.

SUMMARY

A modification of the extrapolation ionization chamber is described in which a spherical phantom is incorporated in order to simulate intracavitary use.

Measurements were made with a small cylindrical source of Ru-Rh^{106}, including determination of an absorption curve and the radiation pattern.

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FILM DOSIMETRY OF ELECTRONS IN THE ENERGY RANGE 0.5 TO 1.4 MEV.*

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1. INTRODUCTION

THE recent advances in radioactivity leading to high activity radiation sources has made the study of personnel monitoring increasingly important. For gamma rays many of the techniques used earlier for roentgen rays have provided development guides. However, since high-activity electron sources have only recently become available, personnel monitoring systems for electrons are somewhat behind those for gamma rays. Several techniques, including photographic films similar to the film badges used for roentgen rays, have been suggested. In the film technique, the opacity of the processed film is a measure of the radiation received by it. However, each type of film requires a calibration curve relating the darkening of the film to the radiation exposure.

Monitoring techniques do not require a high accuracy since the short-time biological responses for low exposures are not appreciable, and, in addition, there are considerable individual variations in radiation response. Usually an accuracy of 15 to 30 per cent is acceptable.[4] It is therefore entirely feasible to determine the ionization produced in an air cavity by the radiation and from this to compute the dose delivered to the surrounding tissue. The theoretical and experimental factors involved in this computation are not accurately known but it is estimated that the overall accuracy of the computation is within 5 per cent.

Because of the high attenuation in the body of the radiation from commonly available electron sources, the dose received near the surface of the skin is most important. However, since the skin has a dead layer averaging 7 mg./cm.^{2}, there is no reason for measuring the dosage at smaller depths. Actually, because of electron scattering, the dosage may increase somewhat beyond this depth but for moderate electron energies personnel monitoring dosages are measured at this depth.

Density-dosage curves for two film, Minimax Dental X-ray Film Extra Fast and duPont Dosimeter film type 552 single film packet,* when exposed to electrons of 0.5 to 1.4 mev. and also to the beta rays from uranium, are presented in the present paper.

The polystyrene used in this experiment has an average atomic number and density close to that of human tissue. In addition, 7 mg./cm.^{2} of polystyrene is used to simulate the dead layer of tissue. Consequently the correlation experiment reported here relates the darkening of the film previously mentioned when exposed to electron bombardment in terms of the energy dissipated in 7 mg./cm.^{2} of polystyrene which is equivalent to the dead layer of human tissue. It must be clearly understood that the dosage is not the energy dissipated in the film but that in the polystyrene. The two are related by way of the relative stopping powers of the material.

2. APPARATUS AND PROCEDURE

High energy electrons produced in an electron accelerator[3] passed through a 20×10^{-4} cm. thick aluminum window into an evacuated

* The Minimax Dental Film may be obtained from the Minimax Company, Chicago, Illinois. The duPont film was a specially prepared film packet used by the Atomic Energy Commission and is no longer available.

* The work described here was sponsored by the Atomic Energy Commission.
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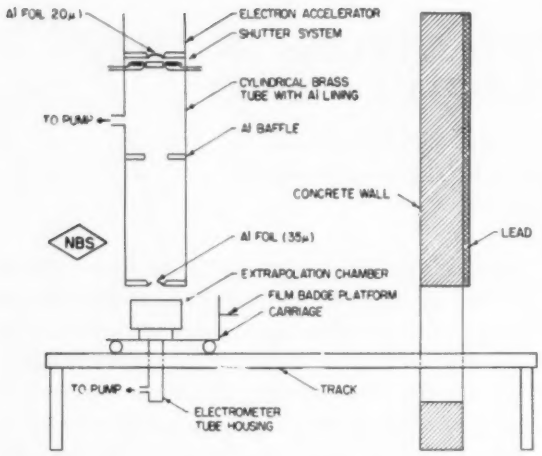

FIG. 1. Arrangement of apparatus showing the extrapolation chamber in position under the electron accelerator.

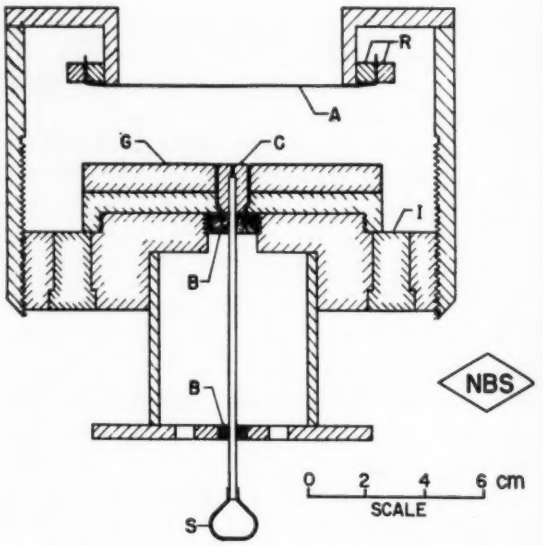

FIG. 2. Cross-sectional drawing of the extrapolation chamber. A = accelerating electrode; B = amber bushings; C = collecting electrode; G = guard ring; R = Bakelite rings; S = phosphor bronze spring; I = Bakelite insulator.

collimator, and thence through a second window into either an ionization chamber or into the film badge. A shutter near the first window permitted accurate control of the film exposure. Aluminum baffles in the collimator served to reduce the amount of scattered radiation incident on the film or ionization chamber and to make the main electron beam parallel. A carriage supported both the film badge holder and the ionization instruments so that either could be accurately positioned in the electron beam (Fig. 1).

The extrapolation type ionization chamber[5] (Fig. 2) was arranged so that the plates were perpendicular to the beam and the spacing could be varied. The plate upon which the electron beam was incident had a thickness of 7 mg./cm.^{2} of polystyrene. The collector plate size (1.04 cm. diameter) was determined to be well within the area of uniform electron beam intensity. An FP-54 electrometer located directly below the chamber measured the ionization current to this collector by indicating the voltage drop across a fixed resistor in the grid circuit.

It has recently been recommended[11] that electron dosages be expressed in terms of energy absorbed per gram of tissue at the position in question. It has been shown[6] that the energy, E_m, absorbed per gram of material is related to the number, $\mathcal{J}_m$, of ion pairs produced in a small air cavity per gram of air by

$$E_m = sW\mathcal{J}_m$$

where s is the stopping power of the material relative to air* and W is the energy required to produce an ion pair (5.2×10^{-11} ergs to within 3 per cent). $\mathcal{J}_m$ is determined from the potential, V (volts), across the grid resistor, 4.56×10^8 ohms, the area of the collector, 0.855 cm.^{2}, the density of air at NTP, 0.00129 g/cm^3, the actual air pressure, P (mm. of Hg), the temperature, T (°K), the electronic charge, 1.60×10^{-19} coulombs, the time, t, and the plate separation, d (cm.). Therefore:

$$E_m = \frac{(1.020)(5.20)(10^{-11})V(760)Tt}{(4.56)(10^8)(0.855)d(0.00129)P(273)(1.6)(10^{-19})} = 1840\,\frac{VtT}{dP}.$$

* Computed values of s vary with electron energy but 1.02 represents a mean value which is probably accurate to ±2 per cent for the energy range of interest here.

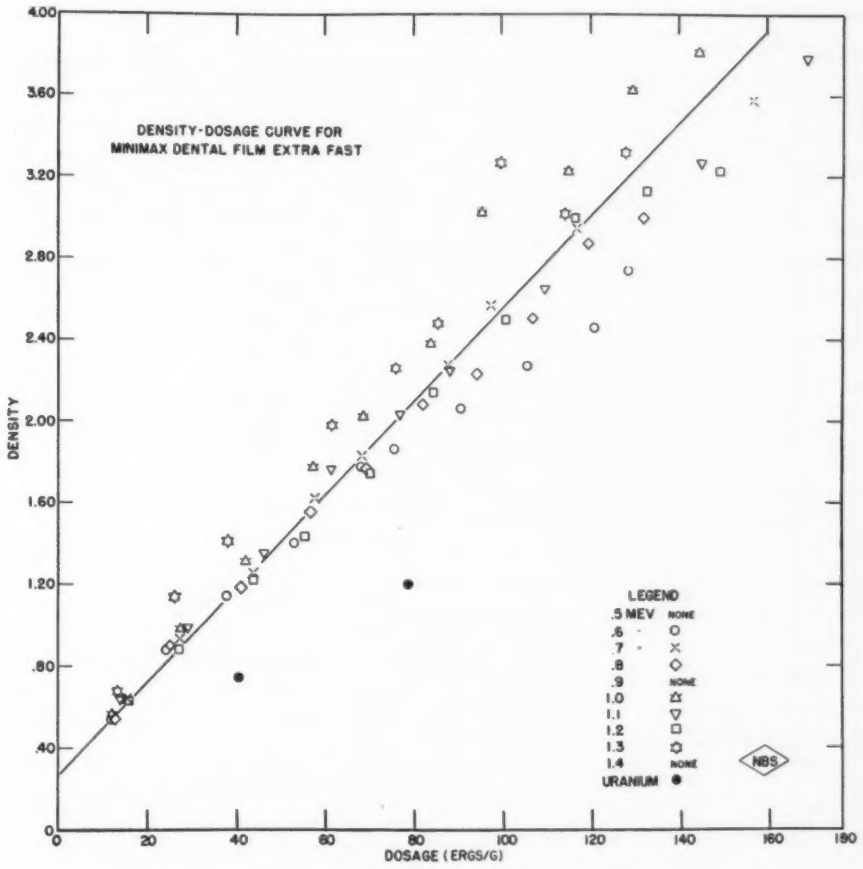

FIG. 3. Density-dosage curves for Minimax Dental X-ray Film Extra Fast

Values of V were obtained experimentally for several different plate separations, d. The slope of the resulting curve gave V/d and this together with the pressure and temperature gave the exposure rate, E_m/t.

Data were obtained at each 0.1 mev. in the range from 0.5 to 1.4 mev. The electron dosage rate was first determined at a given accelerating potential by the ionization chamber. The chamber was removed from the beam and films were exposed to different dosages by timing the exposures. Ionization measurements were then repeated to determine the constancy of the dosage rate. For changes in dosage rate less than 10 per cent, average dosage rates were used; for changes larger than 10 per cent, interpolated dosage rates were used.

Film exposures were also made on a large uranium plaque by placing the film directly on the tight 7 mg./cm.^{2} covering of the plaque. The dosage rate of the plaque had previously been measured* to be 20.1 ergs per gram per hour at the surface of the covering by an extrapolation chamber method.

All films exposed at a given energy plus a control film were processed simultaneously. They were developed for 5 minutes in Eastman Liquid X-ray Developer and Replenisher at 20°C., fixed for 5 minutes at 20°C., washed for 30 minutes, and dried. Film density was determined on a calibrated Ansco-Sweet densitometer, model 11, for densities below 2.5 and on an Ansco color densitometer model 12 for higher densities.

3. RESULTS AND DISCUSSION

Figures 3 and 4 show the results of the density-dosage determination of Minimax and duPont 552 film respectively. In each figure, two sets of curves are presented:

* We are indebted to the New York Operation Office of the Atomic Energy Commission for the loan of this standard and for its calibration constant.

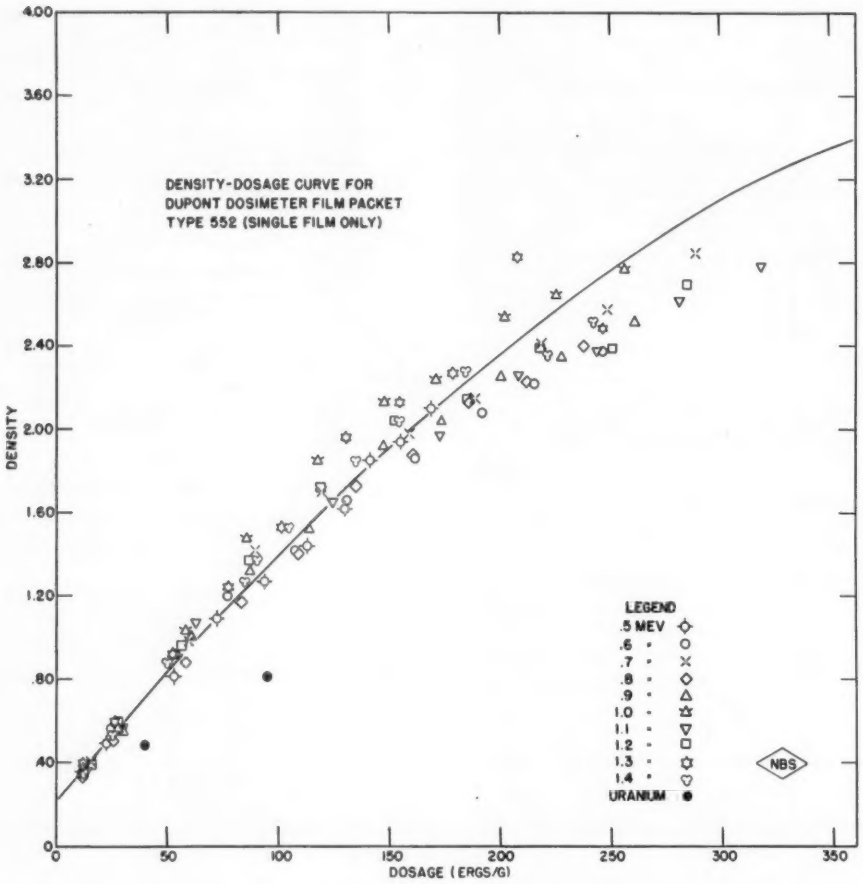

Fig. 4. Density-dosage curves for duPont Dosimeter film type 552 single film packet.

the upper set are the data for the density-dosage relationship by using mono-energetic electrons and the results are plotted using the various values of the incident energy of the electrons as a parameter; the lower curve is the density-dosage relationship by using the uranium plaque. An examination of the data for mono-energetic electrons seems to indicate that the response of these films is independent of the energy. In order to establish this more accurately, the density was plotted against the energy by using several values of the dosage as a parameter (50, 100 and 150 ergs per gram). By the method of least squares, it was determined that to within the accuracy of the results the density-dosage relationship is independent of the energy in the energy interval 0.5 to 1.4 mev. These results can be understood in the following qualitative manner: the dosage to which a film has been exposed is essentially a measure of the amount of energy which has been expended by the electron in its traversal through a film. The main cause of this energy loss results from the inelastic scattering of the electrons by the atoms of the photographic emulsion. However, this process is the mechanism which accounts for the darkening of film. Consequently, to a first approximation one expects a linear dependence of density upon dosage for electrons of sufficient energy to penetrate the film completely.

Pelc[10] has made the most intensive theoretical study of the action of roentgen rays and electrons on photographic film. He shows that the form of the density-dosage relationship is

$$D = D_0(1 - e^{-\epsilon r})$$

where D_0 is the saturation density and r is the dosage in roentgens. The quantity ϵ is a function of the mass of the undeveloped grains, the number of quanta required to affect a grain, and in the case of roentgen rays, the mass absorption coefficient of the silver bromide grains. Expanding the quantity in the exponent, it will be observed that for small values of (ϵr) one must expect a linear function for the density-dosage relationship. In the low density-region, it will be observed that the density does indeed exhibit this linear relationship very well. This independence of the response of the film to electron energy and the linear dependence upon energy loss in the film is of the type to be expected from Pelc's results. As shown by these curves, the slope of the curve is determined only by the type of the film used; *i.e.*, upon grain size, etc. For the duPont 552 film only, there exists a slight amount of curvature for densities greater than 1.0. The saturation density for this film has been determined to be roughly 3.5; thus, the curvature which is observed results from the saturation properties of the film. For Minimax film, this curvature is not observed in the density range zero to six. In the low energy region where the incident electrons are stopped in the film, the response of the film can be expected to be energy dependent.[1,2,8]

The lower curves of Figures 3 and 4 respectively show the response of Minimax and duPont 552 film when exposed to uranium. These curves indicate a slope which is roughly one-half of that of the corresponding curves obtained by using mono-energetic electrons in the previously mentioned energy interval. This difference in slope results from the difference in the energy spectrum to which the films have been exposed. The electrons from the uranium plaque have a continuous spectrum with a calculated most probable energy at roughly 0.1 mev. and an average in the neighborhood of 0.45 mev. In the decay scheme of U^{238} there are six beta emitters of interest, UX_1, UX_2, RaB, RaC, RaD and RaE.[9] Emitters UX_1 and RaC each have two possible modes of decay. For UX_1 the beta spectrum of one of the transitions has a maximum energy of 0.205 mev. and is 80 per cent probable; the other has a maximum energy of 0.11 mev. and is 20 per cent probable. For RaC, the end point energies are 1.65 and 3.16 mev. with a probability of 80 per cent and 20 per cent respectively. The remaining end point energies are 2.3, 0.7, 0.029 and 1.16 mev. respectively. From these data, semi-empirical beta spectra[7] have been constructed for each of these transitions to determine a composite spectrum. In this manner, the above values of the most probable energy and average energy have been determined. The film itself is wrapped in two layers of paper whose total thickness is of the order of 25 mg./cm.^{2} From the curve of the composite U^{238} spectrum it can be shown that the fractional number of electrons absorbed in the paper wrapping is of the order of 22 per cent so that the fractional loss of electrons due to their absorption by the paper covering is large for electrons from uranium and small for electrons from the mono-energetic beam. Consequently, the reduced density of the film when exposed to the uranium plaque results from the loss of electrons by absorption as well as the modification of the electron energy spectrum upon passage through the paper wrapping.

An auxiliary experiment was performed to determine the dependence of the Minimax dental film only upon the energy spectrum of the incident electrons. In addition to the paper wrapping normally present, aluminum absorbers of varying thickness were wrapped around the film and the films were exposed to the uranium plaque until each received a surface exposure equal to 41.9 ergs per gram of tissue-equivalent material. A set of data was obtained by using mono-energetic electrons at 0.6, 0.9 and 1.2 mev. The results of this experiment are shown in Figure 5. The upper

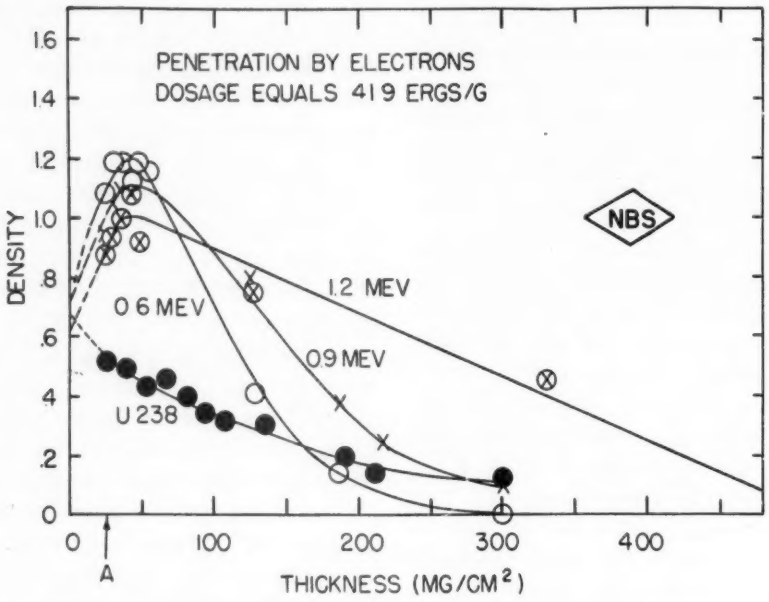

Fig. 5. Electron absorption curves by using aluminum absorbers. A = thickness of paper covering the film.

curves are the results for the density of the film with aluminum absorbers when exposed to mono-energetic electrons at the three energies. The lower curve is the result for the identical experiment using the uranium plaque. For zero aluminum absorber the density of the exposed film after background had been subtracted is approximately 0.52 for the lower curve. This value is to be compared with the density of 0.45 obtained from the corresponding point in Figure 3 when the background of 0.25 is subtracted. In Figure 5, the density of the film for zero aluminum absorber at 0.6 and 1.2 mev is 1.10 and 0.87 respectively. Comparison with 0.9 mev. is omitted since no density-dosage information had been taken at this energy for Minimax film. The densities from Figure 3 at a dosage of 41.9 ergs per gram are 0.90 and 0.95 for the energies 0.6 and 1.2 mev. respectively. The curves of Figure 5 for the mono-energetic electrons give an average density of 0.97 for zero aluminum absorber. This value stands in good agreement with the value of 0.94 obtained from Figure 3.

It is clear from the foregoing results that a simple determination of the density is not sufficient in order to determine uniquely the dosage to which the film has been exposed. In addition to the density, a knowledge of the energy spectrum of the electron beam would be required. In order to circumvent this limitation a step-wedge type of filter could be used. A plot of the filter thickness against film densities would then permit extrapolation to a filter thickness of 7 mg./cm.^{2} Because the thinnest filter would have to be quite thick in order to make the packet light tight and because beta rays and electrons produce very different types of attenuation curves, the proposed filter would not give a high order of accuracy but in many cases it may be sufficient for personnel monitoring.

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A PORTABLE ROENTGEN-RAY STEREOSCOPIC UNIT*†

By CAPTAIN CLIFFORD F. STOREY, MC, USN, LIEUTENANT JOSEPH V. CUSMANO, MC, USNR, *and* DONALD J. LOVE, HM3, USN

THE great advances which have been made in thoracic surgery within the past decade or two have contributed to a striking increase in the utilization of roentgenographic studies of the chest. The frequency with which thoracic exploration is carried out and the wide variety of pulmonary lesions now treated by excisional surgery have enhanced the importance of roentgenographic studies in the precise preoperative evaluation of intrathoracic lesions. In addition, chest roentgenograms are of vital importance in the postoperative management of patients who have been treated by pulmonary resection. In most clinics it is the practice to secure a portable chest roentgenogram as soon as the patient has reacted from the anesthetic sufficiently to be raised to the sitting position, and at least once daily thereafter until the residual lung has fully re-expanded and the suction-drainage tubes have been removed from the chest. Localized air-pockets may require the insertion of additional small catheters, by means of a trocar and cannula, for their evacuation. Fluid collections not accessible to the routine drainage tubes may signalize the necessity for thoracentesis. The detection of significant atelectasis on either the operated side or in the contralateral lung makes clear the need for intratracheal catheter suction, or, if that does not relieve the condition, therapeutic bronchoscopy. It is often important to be able to differentiate areas of pneumonitis from simple pleural reaction.

We do not decry the importance of careful physical examination, particularly auscultation of the chest, in following thoracic surgical patients in the postoperative period. It is not felt, however, that auscultation affords information of the same degree of accuracy as that provided by portable chest roentgenograms. In some patients the information obtained from a single anteroposterior portable chest roentgenogram is not sufficiently precise for proper corrective therapy to be instituted to the best advantage. A single roentgenogram in that projection gives no exact localization of a fluid collection or air-space in the anteroposterior direction. Portable chest roentgenograms in the lateral projection are, in general, of such poor quality as to be virtually useless. This combination of facts has impressed upon us the desirability of being able to obtain satisfactory stereoscopic frontal chest films with a portable machine. For practical purposes, the ability to secure acceptable stereoscopic anteroposterior chest roentgenograms would, it was felt, largely obviate the necessity for lateral films in the early postoperative period. In addition to their value in the postoperative management of thoracic surgical patients, it was believed that an apparatus that would make good bedside stereoscopic films of the chest possible would be of value in an occasional patient in other categories, either medical or surgical, who developed chest complications and who was too ill to be moved to the roentgen department.

At the request of the senior author, two of us (J.V.C. and D.J.L.) set about to devise a piece of apparatus of the type required. It occurred to us that a regular hospital type over-bed table of the adjustable double pedestal type could easily be modified so that the desired films could readily be taken. These modifications were accomplished by one of us (D.J.L.). A description of the construction of the unit and the technique of its use follows.

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† The opinions or assertions contained herein are those of the authors and are not to be considered as official or reflecting the views of the Navy Department or the naval service at large.

Construction of Portable Stereoscopic Unit. The basic elements of the portable chest stereoscopic unit consisted of an ordinary over-bed hospital table* upon which is mounted the cassette changer, as shown in Figures 1 and 2. The cassete changer consists of a section of $\frac{3}{4}$ inch plywood, measuring approximately 2 by 4 feet, which is interlined with $\frac{1}{6}$ inch sheet lead. This product is available commercially. A central port measuring 14 by 17 inches was removed from the plywood board and replaced by plexiglass. Simple hardwood runners were then constructed and fixed to the plywood board to readily contain two cassettes. These can be shifted easily by hand.

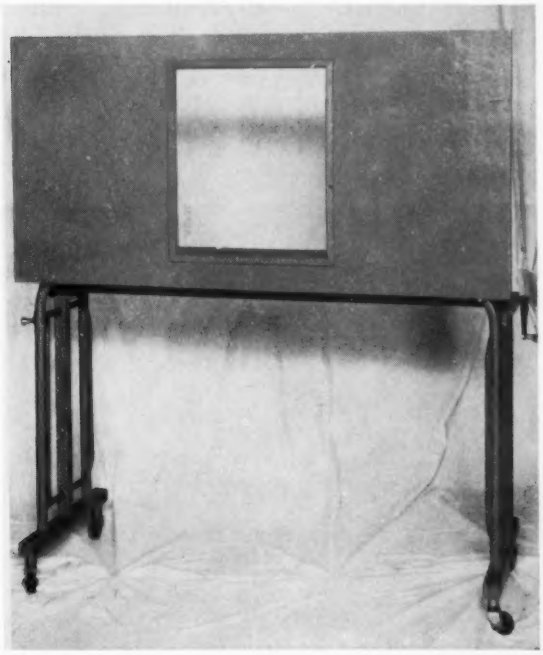

Fig. 1. This is a frontal view of the over-bed table modified for use as a portable stereoscopic cassette holder.

Technique of Stereoscopic Portable Chest Roentgen-Ray Unit. The portable stereoscopic roentgen-ray chest unit is placed in position as shown in Figures 3 and 4. This is accomplished with very little discomfort to the patient. Exposure factors will vary,

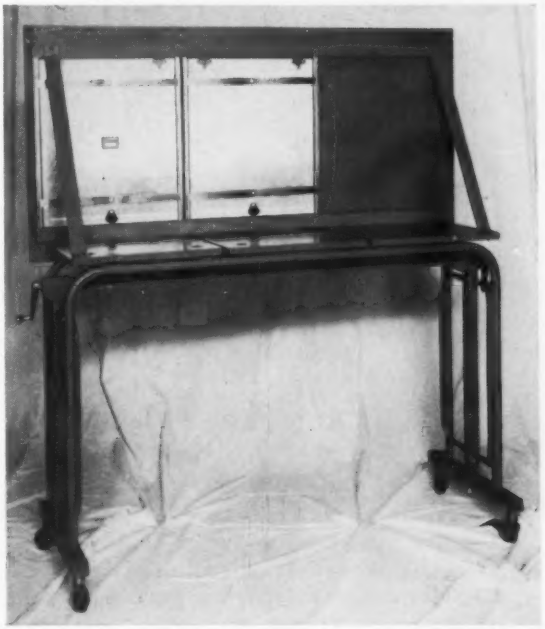

Fig. 2. Posterior view of the over-bed table modified to provide a portable stereoscopic cassette holder.

Fig. 3. The over-bed table has been elevated and is being placed in position for taking anteroposterior stereoscopic chest roentgenograms.

* Manufactured by Doehler Metal Furniture Co., Inc., 192 Lexington Avenue, New York, N. Y., and by Simmons Company, 1 Park Avenue, New York, N. Y.

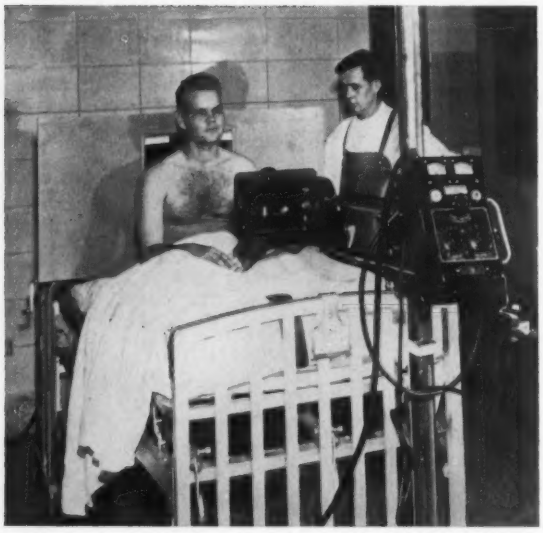

FIG. 4. The cassette holder is now in place and the patient has been raised to the sitting position. The portable roentgen-ray unit is in position for taking the stereoscopic films.

of course, with the particular type of unit used. At this hospital a Mattern portable unit of the 15 milliampere type was used with great success. Units permitting a greater milliamperage, however, would be more advantageous, permitting shorter exposure factors. The tube film distance found to be most satisfactory is 36 inches. The stereoscopic shift is in the vertical plane and consists of a total of 3 inches. Most portable roentgen-ray units will permit such a shift of the tube mount. The tube head is maintained in a horizontal plane.

This unit has given complete satisfaction. Stereoscopic frontal chest films fully comparable in technical quality to those obtained in the main roentgen department can be obtained with it (Fig. 5). It has not been used routinely but, in patients whose

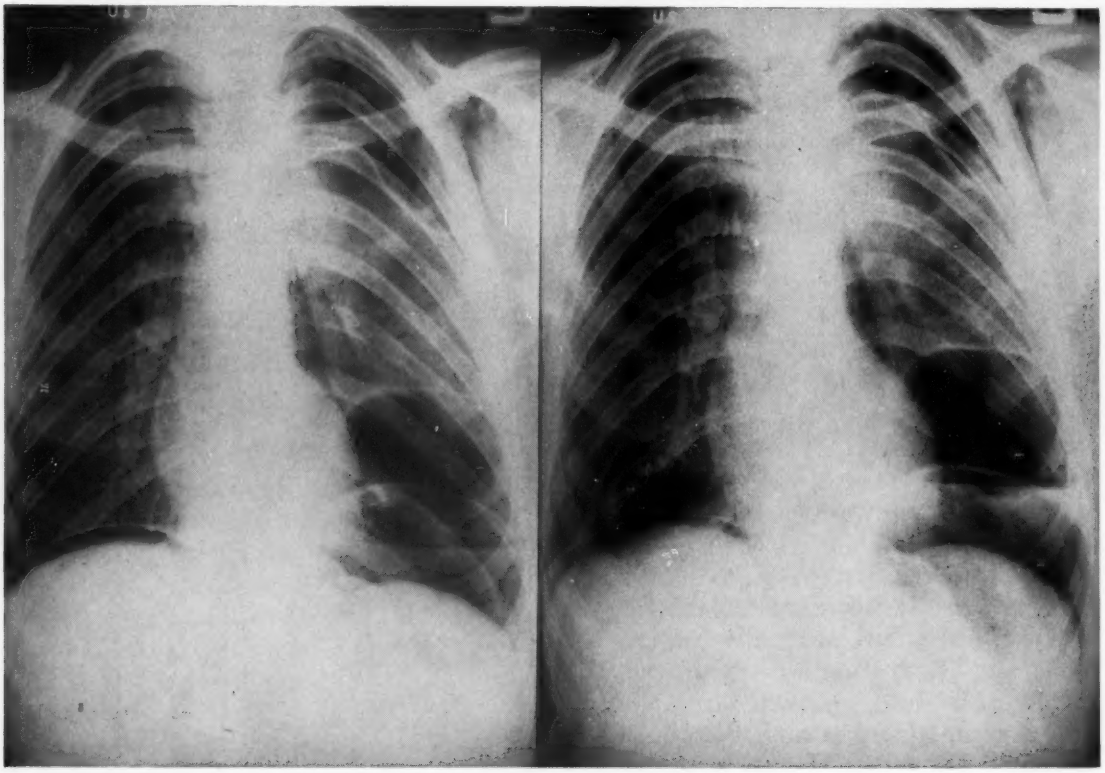

FIG. 5. A stereoscopic pair of chest roentgenograms taken in bed with the portable stereoscopic unit forty-eight hours after segmental resection of the apical-posterior segment of the left upper lobe for pulmonary tuberculosis. The two thoracotomy tubes had been removed twenty-four hours previously, at which time there was no air leak on suction. A late air leak has developed and an apical air space can be seen. There is a much larger air space above the left diaphragm (this patient also has a pneumoperitoneum). An air-fluid level can also be seen at the left base. Stereoscopically, it was clear that the fluid lay posteriorly.

single postoperative portable chest films have shown an abnormality of indefinite location or uncertain character, stereoscopic films obtained with this piece of equipment have been of the greatest assistance in clarifying the nature and localizing exactly the site of the lesion in question. The cassette changer unit is kept on the thoracic surgery wards and untrained ward personnel assist the roentgen technician in taking the films. Being fully portable, the unit can easily be moved to any part of the hospital where its use is required.

SUMMARY AND CONCLUSIONS

An easily constructed, inexpensive and efficient portable roentgen-ray unit which makes stereoscopic portable chest roentgenograms possible has been described. It has proved to be a most useful addition to the roentgen-ray equipment in this hospital. The information obtained from stereoscopic portable chest roentgenograms has contributed to better management of thoracic surgical patients in the early postoperative period. In addition, this apparatus is useful in the precise evaluation of other patients with chest disorders who are too ill to be moved to the roentgen department for roentgenographic examination.

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A METHOD OF RECORDING TIME ON A ROENTGENOGRAM

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IN SERIAL roentgenographic studies the time interval between the exposures is important. It seems curious that no one has yet devised a method of photographing on the roentgen film the time at which it was exposed. While engaged in a study of the rate of absorption of diodrast injected into the intervertebral disc for the purpose of discography, the authors devised a simple method of accomplishing this.

A wrist watch was obtained in which the hands projected beyond the mechanism where they could be seen through the transparent plastic case.* This watch is fastened to the Bucky diaphragm with adhesive tape so that a roentgen picture of the watch appears on each film and denotes the time at which the successive roentgenograms were made. From this, the time interval is readily computed and the sequence of the exposures is indelibly recorded.

The problem of including a similar timepiece in the construction of the Bucky diaphragm would not appear to present insurmountable obstacles. Such a timepiece with a sweep second hand of sufficient roentgen-ray density would record not only the time of day at which the film was made but the duration of the exposure as well.

This note is contributed with the hope that it will stimulate the development of such an apparatus.

Cleveland Clinic
Cleveland 6, Ohio

* The suitability of the "Juvenia" wrist watch was the suggestion of Dr. Otto Glasser.

FIG. 1. A discogram illustrating the principle of photographing the time at which the film was made. (Insert in upper right corner is an actual photograph of the watch.)

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Representatives on National Committee on Radiation Protection: Edith H. Quimby, New York, N. Y., Theodore P. Eberhard, Philadelphia, Pa.

Thirty-seventh Annual Meeting: Shoreham Hotel, Washington, D. C., April 21–23, 1955.

EDITORIAL

LATE MANIFESTATIONS OF INJURIES PRODUCED BY IONIZING RADIATIONS

SINCE the detonation of the first atomic bomb nine years ago, immense interest has developed in the studies of the harmful effects produced by the ionizing radiations. The immediate general and localized biologic alterations which follow the exposure of an individual to various types of radiant energies are now fairly well understood and were commented upon in a former editorial[1] in this JOURNAL. Observation of the late manifestations, however, has had to await the passage of time, although from previous experiences with roentgen rays and radium in both animals and human beings there was good reason to believe that they would eventually occur in greater or lesser degree. These late manifestations may be placed into four groups: (1) physical anomalies in children, (2) premature aging and shortened life span, (3) tumor induction, particularly carcinogenesis and (4) infertility and genetic damage.

Greulich, Crismon and Turner[2] surveyed a series of children who survived the atomic bombing of Hiroshima and Nagasaki, and in August, 1953, published the results of this survey which extended to the end of 1950, *i.e.*, five and one-half years after the bombing. A perusal of these results indicates that very valuable statistical data have been obtained relative to some late manifestations of ionizing radiations as enumerated above. This is true in particular as regards the physical growth and development of the children, which in fact constituted the main purpose of their study.

Greulich and his co-workers, in selecting the exposed children in Hiroshima and Nagasaki, tried to include only those who had a definite history of epilation and radiation illness following the atomic bombing. This attempt was not entirely successful, however, since in some instances this history was denied later by the parents or their surviving relatives. As controls they used a similar series of children from Kure and Sasebo, corresponding in number and age distribution to those in the exposed series of Hiroshima and Nagasaki. In 1948, the Sasebo children were replaced by "internal control children" from Nagasaki who had not been there at the time of the atomic explosion and consequently were not exposed. The principal factors studied were the height, weight and skeletal status of the children. The methods used consisted of anthropometric measurements, roentgenograms of the hand, wrist, and of various other joint areas and serial photographs made at successive examinations.

Greulich and his co-workers concluded, from this very exhaustive survey, that there was a definite retardation in the height, weight and skeletal development of the exposed children as compared to the nonexposed controls. This retardation was still evident at the end of 1950, when the Hiroshima children and those of the Nagasaki exposed group showed average heights and weights which children of the same sex and age in Japan as a whole had achieved by 1946 and 1947. In general, the boys were more retarded than the girls of the same groups. It is emphasized, however, that other factors besides the ionizing radiations might have had their share in influencing the adverse physical growth

[1] Leucutia, T. Radiant energy injuries. Editorial. AM. J. ROENTGENOL. & RAD. THERAPY, 1948, *59*, 890–893.

[2] Greulich, William W., Crismon, Cathrine S., and Turner, Margaret L. Physical growth and development of children who survived the atomic bombing of Hiroshima or Nagasaki. *J. Pediat.*, 1953, *43*, 121–145.

and development of these children. Enumerated among these are the harmful action of thermal and other types of radiation emitted during the atomic explosion; the physical and psychological injuries incurred from the explosion; the subsequent severe disruption of the economy resulting in widespread poverty and malnutrition; and possibly some other evils that follow in the wake of such a cataclysm.

Greulich and his co-workers also made the important observation that in some of the exposed children the wounds had not as yet healed, five and one-half years after the atomic explosion which had produced them. These wounds undoubtedly are the direct sequelae of thermal burns and of the effect of ionizing radiations, both of which are known to induce cancer in a significant number of cases. Two serious questions are posed, therefore; first, will these children in time develop some form of malignant neoplasia at the site of the unhealed wounds and second, if so, will the double insult, which many of these children have received, produce an appreciable increase in the frequency of malignant degeneration as compared with the response to either type of injury alone? The Atomic Bomb Casualty Commission has already reported[3] what appears to be a real increase in the incidence of leukemia in the survivors of Hiroshima and Nagasaki as a whole.

Another important question, although of greater concern to posterity than our generation or even the next few generations is the genetic damage produced by the irradiation in these children. If the amount of exposure reaching the gonads was sufficiently large, permanent sterility may follow and the passage of time will determine this. If, however, the dose was less excessive, it is conceivable that genetic changes will appear in their offspring. Muller,[4] the eminent geneticist who for more than a quarter century has made outstanding contributions to the literature on many aspects of the genetic damage induced by roentgen rays, gave an excellent discussion of some of the major points relating to this subject on January 3, 1953, at a symposium presented before the New York Obstetrical Society. The topic of this symposium was whether roentgen irradiation of the ovaries used for the induction of ovulation in apparently sterile women represents any danger to their progeny. Such a procedure has been successfully employed for many years by Kaplan and his followers and by a few other radiologists. At the same symposium Kaplan[5] presented his follow-up results in 270 out of 660 infertile women who were treated with low doses of high voltage roentgen therapy during a period of twenty-eight years and who subsequently gave birth to 347 children who were normal in every respect. Of 34 of these children whose mothers were treated more than twenty years ago, 20 have married and produced normal living children, that is, grandchildren of the mothers originally irradiated for sterility. On the basis of this study, Kaplan expresses the opinion that roentgen irradiation of the ovaries with small doses as advocated for induction of ovulation produces no adverse genetic effect in the second or third generation of such women and consequently it carries no danger to her progeny's offspring.

Muller,[4] on the other hand, states that there is no doubt that detrimental mutations are produced in highly significant numbers by the irradiation of the ovaries with the advocated dosage. It is erroneous to believe, according to him, that mutations are more likely to show in the second generation than in the first. The long-range damage is the one that counts and this depends on the total number of detrimental mutations produced as a whole, the frequency of the mutations induced by the irradiation being proportional to the magnitude of the dose received by the gonads.

[3] Major Activities in Atomic Energy Programs. U. S. Atomic Energy Commission Report, Jan.–June, 1951. Supt. of Documents, Government Printing Office, Washington 25, D. C., p. 42.

[4] Muller, H. J. Damage to posterity caused by irradiation of gonads. *Am. J. Obst. & Gynec.*, 1954, *67*, 467–483.

[5] Kaplan, Ira I. Third generation follow-up of women treated by x-ray therapy for menstrual dysfunction and sterility twenty-eight years ago, with detailed histories of grandchildren born to these women. *Am. J. Obst. & Gynec.*, 1954, *67*, 484–490.

The observations of Muller were made on *Drosophila melanogaster* since this fruit fly is admirably suited for long-range genetic studies. It can be bred under controlled conditions and the variations in numerous characteristics produced by the irradiation can be easily distinguished. Because of the brief life span, many generations can be studied in a short time and a very large number of the flies can be accommodated in a small space.

The investigations were quickly extended by subsequent workers to many other organisms as far down in the scale as the viruses, across to plants as far as the fungi and up the animal kingdom to the mammals. Of special interest in this respect are studies of Russell[6] made in mice, since the results obtained represent the nearest approximation at present to similar effects in man. Russell performed extensive experiments on mutations produced by roentgen rays in seven specific genes of mice. He demonstrated that a dose of 80 roentgens induces one mutation in 50,000 gametes of a given gene in mice, which corresponds to the rate of spontaneous mutations occurring in man and is considerably higher than the frequency of spontaneous mutations per individual gene observed in *Drosophila melanogaster*.

Muller,[7] on the basis of these findings, assumes that if a similar dose of roentgen rays or any other type of ionizing radiation induces the same mutation rate in man, a doubling of the spontaneous production of mutations would ensue with the result that, if continued indefinitely, a "genetic death" would occur in 2 out of 5 persons. He also states that such a situation would cause a 40 per cent (instead of the usual 20 per cent) reduction in the fitness of the average individual and that, if it persisted indefinitely, would lead to continued genetic deterioration and/or continued decline in numbers.

This indicates, in Muller's estimation, that irradiation of the pelvic region for induction of ovulation causes much greater total harm to later generations than to the exposed individual herself.

From the point of view of genetic damage, it is questionable whether even the presently accepted "permissible dose" of radiation of 0.3 r per week can be considered entirely safe. A dose of 80 r would be received in sixty-four months if the person were exposed to 0.3 r per week. Yet, according to Russell's experiments, this amount would double the spontaneous mutation if spread over an entire life span. Since the span of the reproductive period in man is assumed to be twenty-six years, the total dose, at the rate of 0.3 r per week, would reach during this period 400 r. Therefore, Muller[7] believes that the "permissible dose" may be allowed to remain at 0.3 r per week for decades only for the relatively few persons who are occupationally exposed to radiation. The average per capita permissible dose should be much smaller. As a provisional measure he recommends that the total dose to which the gonads of an individual may be exposed before reproduction be limited to about 20 r. This would result in only one-fourth increase of the spontaneous mutation rate.

It is obvious that observations over very long periods, even several generations, are necessary before all these ill-bounded and very ramifying problems can factually be ascertained. The slowly and painstakingly gathered evidence, however, points with ever-increasing certainty to the fact that harmful effects are being produced by ionizing radiations in several ways which have not been fully appreciated. Since rapidly developing progress in the use of atomic energy brings with it more and more exposure to ionizing radiations, the child of the future may face a situation which even at this early stage should not be ignored.

T. LEUCUTIA, M.D.

[6] Russell, W. L. X-ray induced mutations in mice. Cold Spring Harbor Symp. Quant. Biol. The Biological Laboratory, Cold Springs Harbor, L. I., New York, 1951, Vol. XVI (1952), 327.

[7] Muller, H. J. Manner of dependence of "permissible dose" of radiation on amount of genetic damage. *Acta radiol.*, 1954, *41*, 5–20.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

MEETINGS OF ROENTGEN SOCIETIES*

United States of America

American Roentgen Ray Society
Secretary, Dr. Barton R. Young, Germantown Hospital, Philadelphia 44, Pa. Annual meeting: Shoreham Hotel, Washington, D.C., Sept. 21–24, 1954.

American Radium Society
Secretary, Dr. R. E. Fricke, Mayo Clinic, Rochester, Minn. Annual meeting: Shoreham Hotel, Washington, D. C., April 21–23, 1955.

Radiological Society of North America
Secretary, Dr. D. S. Childs, 713 E. Genesee St., Syracuse 2, N. Y. Annual meeting: Biltmore Hotel, Los Angeles, Calif., Dec. 5–10, 1954.

American College of Radiology
Executive Secretary, William C. Stronach, 20 N. Wacker Drive, Chicago 6, Illinois.

Section on Radiology, American Medical Association
Secretary, Dr. T. Leucutia, Harper Hospital, Detroit 1, Mich. Annual meeting: San Francisco, Calif., June 21–25, 1954.

Fifth Inter-American Congress of Radiology
General Secretary, Dr. Eugene P. Pendergrass, 3400 Spruce St., Philadelphia 4, Pa. Meets at Shoreham Hotel, Washington, D. C., April 24–29, 1955.

Alabama Radiological Society
Secretary, Dr. J. A. Meadows, Jr., Medical Arts Bldg., Birmingham 5, Ala. Meets time and place Alabama State Medical Association.

Arizona Radiological Society
Secretary, Dr. R. Lee Foster, 507 Professional Bldg., Phoenix, Ariz. Two regular meetings a year. The annual meeting at time and place of State Medical Association and interim meeting six months later.

Arkansas Radiological Society
Secretary, Dr. Fred Hames, 511 National Bldg., Pine Bluff, Ark. Meets every three months and also at time and place of State Medical Association.

Atlanta Radiological Society
Secretary, Dr. Albert A. Rayle, Jr., 478 Peachtree St., N.E., Atlanta, Ga. Meets monthly, except during three summer months, on second Friday evening.

Brooklyn Roentgen Ray Society
Secretary, Dr. J. J. Daversa, 345 75th St., Brooklyn, N.Y. Meets monthly fourth Tuesday, October through April.

Buffalo Radiological Society
Secretary, Dr. Mario C. Gian, 610 Niagara St., Buffalo, N. Y. Meets second Monday evening each month, October to May inclusive.

Central New York Roentgen Ray Society
Secretary, Dr. Dwight V. Needham, 608 E. Genesee St., Syracuse N. Y. Meets January, May, November.

Central Ohio Radiological Society
Secretary, Dr. F. A. Riebel, 15 West Goodale St., Columbus, Ohio. Meets at 6:30 P.M. on second Thursday of October, December, February, April, and June at Columbus Athletic Club, Columbus, Ohio.

Chicago Roentgen Society
Secretary, Dr. Elbert K. Lewis, 6337 S. Harvard Ave., Chicago, Ill. Meets second Thursday of each month, October to April inclusive at the University Club.

Cleveland Radiological Society
Secretary, Dr. Mortimer Lubert, 10515 Carnegie Ave., Cleveland 6, Ohio. Meetings at 6:45 P.M. on fourth Monday of each month from October to April.

olorado Radiological Society
Secretary, Dr. Parker Allen, Children's Hospital, Denver, Colo. Meets third Friday of each month at University of Colorado Medical Center or at Denver Athletic Club.

Connecticut Valley Radiologic Society
Secretary, Dr. E. W. Godfrey, 1676 Boulevard, West Hartford, Conn. Meets second Friday October and April.

Dallas-Fort Worth Radiological Club
Secretary, Dr. O. H. Grunow, 650 Fifth Ave., Fort Worth, Texas. Meets monthly, third Monday, at Greater Fort Worth International Airport at 6:30 P.M.

Detroit Roentgen Ray and Radium Society
Secretary, Dr. E. F. Lang, Harper Hospital, Detroit, Mich. Meets monthly first Thursday, October to May, at Wayne County Medical Society Building.

East Bay Roentgen Society
Secretary, Dr. Dan Tucker, 434 30th St., Oakland 9, Calif. Meets first Thursday each month at Peralta Hospital, Oakland.

Florida Radiological Society
Secretary, Dr. H. G. Reaves, Medical Arts Bldg., Sarasota, Fla. Meets twice annually, in the spring with the annual State Society meeting, and in the fall.

Georgia Radiological Society
Secretary, Dr. Robert M. Tankesley, 218 Doctors Bldg., Atlanta, Ga. Meets in mid-winter and at annual meeting of Medical Association of Georgia in the spring.

Greater Miami Radiological Society
Secretary, Dr. R. D. Shapiro, 541 Lincoln Rd., Miami Beach, Fla. Meets monthly at various South Florida Hospitals.

Houston Radiological Society
Secretary, Dr. Harry Fishbein, 324 Medical Arts Bldg., Houston 2, Texas. Meets fourth Monday each month at Hermann Hospital.

Idaho State Radiological Society
Secretary, Dr. Alfred M. Stone, St. Lukes Hospital, Boise, Idaho. Meets annually at same time as Idaho State Medical Association.

Illinois Radiological Society
Secretary, Dr. Stephen L. Casper, 1101 Maine St., Quincy, Ill. Meets three times a year.

Indiana Roentgen Society
Secretary, Dr. William M. Loehr, 712 Hume-Mansur Bldg., Indianapolis 4. Meets second Sunday in May.

Iowa Radiological Society
Secretary, Dr. James T. McMillan, 1104 Bankers Trust Bldg., Des Moines, Iowa. Luncheon and business meeting during annual session of Iowa State Medical Society. The scientific section is held in the autumn.

Kansas Radiological Society
Secretary, Dr. A. M. Cherner, Hays, Kansas. Meets in spring with State Medical Society, and in winter on call.

Kentucky Radiological Society
Secretary, Dr. David Shapiro, 323 East Chestnut St., Louisville 2, Ky. Meets monthly on second Friday at Seelbach Hotel, Louisville.

Kings County Radiological Society
Secretary, Dr. Solomon Maranov, 1450 51st St., Brooklyn 19, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:45 P.M.

Los Angeles Radiological Society
Secretary, Dr. George Jacobson, 1200 N. State St., Los Angeles 33, Calif. Meets second Wednesday each month at Los Angeles County Medical Association Building, Los Angeles.

* Secretaries of societies are requested to send timely information promptly to the Editor.

MAINE RADIOLOGICAL SOCIETY
Secretary, Dr. Jack Spencer, Maine General Hospital, Portland 4, Maine. Meets in early spring, June and fall.

MARYLAND RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Maryland.

MIAMI VALLEY RADIOLOGICAL SOCIETY
Secretary, Dr. G. A. Nicoll, 134 Apple St., Dayton, Ohio. Meets second Friday of fall and winter months.

MID-HUDSON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Walton, Horton Memorial Hospital, Middletown, N. Y. Meets 8:30 P.M., fourth Tuesday each month, September to May.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. T. J. Pfeffer, 839 N. Marshall St., Milwaukee 2, Wis. Meets monthly on second Monday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Hodgson, Mayo Clinic, Rochester, Minn. Meets three times annually, once at time of State Med. Assn., and in spring and fall.

MISSISSIPPI RADIOLOGICAL SOCIETY
Secretary, Dr. John W. Evans, 117 N. President St., Jackson, Miss. Meets third Thursday of each month at the Rotisserie Restaurant at 6:30 P.M.

MONTANA RADIOLOGICAL SOCIETY
Secretary, Dr. Grant P. Raitt, Suite 413 Medical Arts Bldg., Billings, Montana. Meets at least once a year.

NASSAU RADIOLOGICAL SOCIETY
Secretary, Dr. Frank Huber, Hempstead, N. Y. Meets second Tuesday of the month in February, April, June, October and December.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. J. F. Kelly, Jr., 816 Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. Stanley M. Wyman, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Harvard Club.

NEW HAMPSHIRE ROENTGEN RAY SOCIETY
Secretary, Dr. A. C. Johnston, Elliott Community Hospital, Keene, N. H. Meets four to six times yearly.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. J. R. Freid, 1049 Park Ave., New York 28, N. Y. Meets monthly on third Monday, New York Academy of Medicine, at 8:30 P.M.

NORTH CAROLINA RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Sternbergh, Charlotte Memorial Hospital, Charlotte, N. C. Meets in May and October.

NORTH DAKOTA RADIOLOGICAL SOCIETY
Secretary, Dr. C. O. Heilman, 807 Broadway, Fargo. Meetings by announcement.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY
Secretary, Dr. D. H. Baxter, Albany Hospital, Albany, N. Y. Meets in Albany area on second Wednesdays of October, November, March and April.

NORTHERN CALIFORNIA RADIOLOGICAL SOCIETY
Secretary, Dr. H. B. Stewart, 2920 Capitol Ave., Sacramento, Calif. Meets at dinner last Monday of each month, September to June.

OHIO STATE RADIOLOGICAL SOCIETY
Secretary, Dr. M. M. Thompson, 316 Michigan St., Toledo, Ohio. Annual meeting, Toledo, Ohio, May 22 and 23, 1954.

OKLAHOMA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. John R. Danstrom, Medical Arts Bldg., Oklahoma City, Okla. Three regular meetings annually.

OREGON RADIOLOGICAL SOCIETY
Secretary, Dr. J. W. Loomis, 919 Taylor St. Bldg., Portland 5, Oregon. Meets monthly from October to June on the second Wednesday of each month at 8:00 P.M. at the University Club.

ORLEANS PARISH RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph V. Schlosser, Charity Hospital, New Orleans 13, La. Meets first Tuesday of each month.

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY
Secretary, Dr. S. J. Hawley, 1320 Madison St., Seattle 4, Wash. Meets annually in May.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. J. M. Converse 416 Pine St., Williamsport. Next annual meeting at Bedford Springs Hotel, Bedford, Penna., May 14 and 15, 1954.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. H. M. Stauffer, Temple University Hospital, Philadelphia 40, Pa. Meets first Thursday of each month, at 5 P.M., from October to May in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. Donald H. Rice, Western Pennsylvania Hospital, Pittsburgh 24, Pa. Meets 6:00 P.M. at Webster Hall Hotel on second Wednesday each month, October to May inclusive.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. H. Leonard Warres, 2337 Eutaw Place, Baltimore 17, Md. Meets third Tuesday each month, September to May, inclusive.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. William A. Goodrich, 85 Jefferson St., Hartford 6, Conn. Meetings are held bi-monthly.

RADIOLOGICAL SECTION, MEDICAL SOCIETY OF THE DISTRICT OF COLUMBIA
Secretary, Dr. A. C. Wyman, 5445—28th St., N.W., Washington, D. C. Meets Medical Society Library, third Wednesday of January, March, May and October at 8:00 P.M.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

RADIOLOGICAL SOCIETY OF GREATER CINCINNATI
Secretary, Dr. Chapin Hawley, 927 Carew Tower, Cincinnati 2, Ohio. Meets monthly from September to June on first Monday of each month at 7:30 P.M. at the Cincinnati General Hospital.

RADIOLOGICAL SOCIETY OF HAWAII
Secretary, Dr. P. S. Arthur, Young Hotel Bldg., Honolulu 13, T. H. Meets third Friday of each month at a place designated by the Secretary.

RADIOLOGICAL SOCIETY OF KANSAS CITY
Secretary, Dr. Arthur B. Smith, 800 Argyle Bldg., Kansas City, Mo. Meets third Thursday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA
Secretary, Dr. J. T. Brierre, 700 Audubon Bldg., New Orleans. Meets annually during Louisiana State Medical Society Meeting.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. Salomon Silvera, 921 Bergen Ave., Jersey City, N. J. Meets at Atlantic City at time of State Medical Society and in November in Newark, N. J.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA
Secretary, Dr. Donald R. Laing, 65 N. Madison Ave., Pasadena 1, Calif.

RICHMOND COUNTY RADIOLOGICAL SOCIETY
Secretary, Dr. W. F. Hamilton, Jr., University Hospital, Augusta, Ga. Meets first Thursday of each month at various hospitals.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Henry H. Forsyth, Jr., 40 Meigs St., Rochester, N. Y. Meets at 8:15 P.M. on the last Monday of each month, September through May, at Strong Memorial Hospital.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY
Secretary, Dr. John H. Freed, 4200 East Ninth St., Denver 7, Colo. Meets at Shirley-Savoy Hotel, Denver, Colo., Aug. 19–21, 1954.

St. Louis Society of Radiologists
Secretary, Dr. W. B. Seaman, 510 South Kingshighway, St. Louis 10, Mo. Meets fourth Wednesday each month, except June, July, August and September.

San Antonio-Military Radiological Society
Secretary, Dr. Hugo F. Elmendorf, Jr., 730 Medical Arts Bldg., San Antonio 5, Texas. Meets Brook Army Medical Center Officers Mess first Monday of each month.

San Diego Radiological Society
Secretary, Dr. C. W. Bruner, 2456 Fourth Ave., San Diego 1, Calif. Meets first Wednesday of each month at the University Club.

San Francisco Radiological Society
Secretary, Dr. I. J. Miller, 2680 Ocean Avenue, San Francisco 27, Calif. Meets quarterly.

Section on Radiology. California Medical Association
Secretary, Dr. H. R. Morris, 1027 "D" St., San Bernardino, Calif.

Section on Radiology, Illinois State Medical Society
Secretary, Dr. George E. Irwin, Jr., 703 N. East St., Bloomington, Ill.

Shreveport Radiological Club
Secretary, W. R. Harwell, 608 Travis St., Shreveport, La. Meets monthly on third Wednesday, at 7:30 P.M. September to May inclusive.

South Bay Radiological Society
Secretary, Dr. J. J. McCort, Santa Clara County Hospital, San Jose, Calif. Meets second Wednesday each month.

South Carolina Radiological Society
Secretary, Dr. William A. Klauber, Self Memorial Hospital, Greenwood, S. C. One meeting with South Carolina Medical Association in May, others arranged by President.

Tennessee Radiological Society
Secretary, Dr. G. K. Henshall, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. R. P. O'Bannon, 650 Fifth Ave., Fort Worth 4, Texas.

Tri-State Radiological Society
Secretary, Dr. S. N. Tager, 219 Walnut St., Evansville, Ind. Meets last Wednesday of Oct., Jan., March and May, 8:00 P.M. at Elks' Club in Evansville.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7:00 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets first and third Thursdays 4:00 to 5:00 P.M., September to May, Service Memorial Institute.

Utah State Radiological Society
Secretary, Dr. Angus K. Wilson, 343 S. Main St., Salt Lake City 1, Utah. Meets fourth Wednesday in January, March, May, September and November at Holy Cross Hospital.

Virginia Radiological Society
Secretary, Dr. P. B. Parsons, Norfolk General Hospital, Norfolk, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. Eva L. Gilbertson, 1317 Marion St., Seattle 4, Wash. Meets fourth Monday of each month from September through May at 610 Pine St., Seattle.

West Virginia Radiological Society
Secretary, Dr. W. Paul Elkin, 515 Medical Arts Bldg., Charleston, W. Va. Meets concurrently with annual meeting of West Virginia State Medical Society; other meetings arranged by program committee.

Westchester Radiological Society
Secretary, Dr. M. G. Priestman, New Rochelle Hospital, New Rochelle, N.Y. Meets on third Tuesday of January and October and on two other dates.

Wisconsin Radiological Society
Secretary, Dr. W. W. Moir, 309 Geele Ave., Sheboygan, Wis. Special meetings held during year; annual meeting each spring at Madison, Wis.

X-Ray Study Club of San Francisco
Secretary, Dr. Wm. W. Saunders, Veterans Administration Hospital, San Francisco 21, Calif. Meets monthly, third Thursday, at 7:45 P.M., Lane Hall, Stanford University Hospital.

Cuba, Mexico, Puerto Rico and Central America

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

Sociedad Mexicana de Radiología, A. C.
Secretary General, Dr. Eugenio Toussaint, Calle del Oro No. 15, Mexico 7, D.F. Meets first Monday of each month.

Asociación Puertorriqueña de Radiología
Secretary, Dr. Rafael A. Blanes, Ave. Ponce de Leon 1175, Santurce, P. R.

Sociedad Radiológica Panameña
Secretary, Dr. L. Arrieta Sanchez, Apartado No. 86, Panama, R. de P. Meets monthly in a department of radiology of a local hospital, chosen at preceding meeting.

British Empire

Association of Radiologists of the Province of Quebec
Secretary, Dr. J.-P. Jean, 4039 Tupper St., Westmount, Que.

British Institute of Radiology Incorporated with the Röntgen Society
Ordinary meeting, on the Thursday preceding the third Friday, October to May at 8:15 P.M.
Medical Members' meeting, on third Friday in each month at 5:00 P.M., 32 Welbeck St., London, W 1.

Faculty of Radiologists
Honorary Secretary, Dr. J. F. Bromley, 45, Lincoln's Inn Fields, London, W.C.2, England.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets third Friday each month at 4:45 P.M. at the Royal Society of Medicine, 1 Wimpole St., London.

Canadian Association of Radiologists
Honorary Secretary-Treasurer, Dr. D. L. McRae, Suite 305, 1555 Summerhill Avenue, Montreal 25, Que. Meetings January and June.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext. Halifax, N. S.

Société Canadienne-Française d'Electro-Radiologie Médicales
General Secretary, Dr. Ls Ivan Vallée, 1058 rue St-Denis, Montreal 18, Canada. Meets third Saturday each month.

College of Radiologists (Australia and New Zealand)
Honorary Secretary, Dr. Alan R. Colwell, c/o British Medical Agency, 135 Macquarie St., Sydney, N.S.W.

South America

Asociacion Argentina de Radiologia
Secretary, Dr. Lidio G. Mocsa, Avda. Gral. Paz 151, Córdoba, Argentina. Meetings held monthly.

Sociedad Argentina de Radiologia, Junta Central, Buenos Aires
Secretary, Dr. Oscar F. Noguera, Santa Fe 1171, Buenos Aires. Meetings are held monthly.

Sociedad Argentina de Radiologia, Filial del Litoral, Sede, Rosario
President, Dr. Francisco P. Cifarelli. Meets monthly second Wednesday, 19 ha 663 Italia St., Rosario, Santa Fe.

Sociedad Argentina de Radiologia, Filial del Sur, Sede, La Plata
President, Prof. Dr. Jose P. Uslenghi, La Plata. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Centro Sede, Cordoba
President, Prof. Dr. David L. Caro, Corro 86, Cordoba. Meets monthly.

Sociedad Argentina de Radiologia, Filial del Norte, Sede, Tucuman
President, Dr. Julio Mendez Valladares, Rivadavia 358, Tucuman. Meets monthly.

Sociedad Argentina de Radiologia, Filial de Cuyo Sede, Mendoza.
President, Dr. J. A. Orfila, Hospital Central, Mendoza. Meets monthly.

Sociedade Brasileira de Radiologia Medica
Secretary, Dr. Nicola Caminha, Av. Mem de Sa, Rio de Janeiro, Brazil. Meets monthly, except during January, February and March.

Sociedade Brasileira de Radioterapia
Secretary, Dr. Oscar Rocha von Pfuhl, Av. Brigadeiro Luiz Antonio, 644 São Paulo, Brazil. Meets monthly on second Wednesday at 9:00 P.M. in São Paulo at Av. Brigadeiro Luiz Antonio, 644.

Sociedad Colombiana de Radiologia
Secretary, Dr. Luis E. Lozano B., Carrera 12 No. 20–69, 6° piso, Bogota, Colombia. Meets last Thursday of each month.

Sociedad Peruana de Radiologia
Secretary, Dr. Julio Bedoya Paredes, Apartado 2306, Lima, Peru. Meets monthly except during January, February and March, at Asociación Médica Peruana "Daniel A. Carrión," Villalta, 218, Lima.

Sociedad de Radiologica, Cancerologia y Fisica Medica del Uruguay
Secretary, Dr. Arias Bellini, Av. Agraciada 1464, Piso 13, Montevideo, Uruguay.

Continental Europe

Société Belge de Radiologie
General Secretary, Dr. S. Masy, 111 Avenue des Allies, Louvain, Belgium. Meets monthly, second Sunday at Maison des Médecins, Brussels.

Société Française d'Electro-Radiologie Médicale, and its branches: Société du Sud-Ouest, du Littoral Méditerranéen, du Centre et du Lyonnais, de l'Ouest, de l'Est, et d'Alger et d'Afrique du Nord
Secretary-General, Dr. A. Dariaux, 9 bis, Boulevard Rochechouart, Paris IX°, France.

Ceskoslovensk společnost pro rëntgenologii a Radiologii v Praze
Secretary, Dr. Roman Bláha, Praha XII, stát. nemocnice, Czechoslovakia. Meets monthly except during July, August, and September. Annual general meeting.

Deutsche Röntgen-Gesellschaft
Secretary, Dr. med. Peter Kröker, Evangelisches Krankenhaus, Huyssens Stiftung, (22a) Essen. Annual meeting, Sept. 5–8, 1954, Wiesbaden, Germany.

Societa Italiana di Radiologia Medica
Secretary, Prof. Mario Ponzio, Ospedale Mauriziano. Torino, Italy. Meets biannually.

Nederlandse Vereniging voor Electrologie en Roentgenologie
Secretary, Dr. B. J. Rethmeier, Bornsestraat 378, Almelo, Netherlands.

Polish Society of Radiology
Secretary, Dr. L. Zgliczynski, 59 Nowogrodzka St., Warsaw, Poland.

Gdansk Section, Polish Society of Radiology
Secretary, Dr. A. Smigielska, Akademia Lekarska, Gdansk. Meets monthly last Sunday at 10:30, X-Ray Dept.. Akademia Gdansk.

Wroclaw Section Polish Society of Radiology
Secretary, Dr. R. Marciniak, Akad. Medyczna Wrocław, 68 Curie-Skłodowska St., Wrocław, Poland. Meets first Sunday of each month, X-Ray Department, Akademia Medyczna Wrocław.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banual Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad
USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association.

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Schweizerische Röntgen-Gesellschaft (Société Suisse de Radiologie)
Secretary, Dr. Max Hopf, Effingerstrasse 47, Bern, Switzerland.

India

Indian Radiological Association
Secretary, Dr. R. F. Sethna, Navsari Building, Hornby Road, Bombay 1, India.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

The Rocky Mountain Radiological Society will hold its Mid-Summer Radiological Conference at the Shirley-Savoy Hotel, Denver, Colorado, August 19, 20, and 21, 1954. The Program Committee is arranging an excellent program. The following will be the guest speakers: Dr. Traian Leucutia, Detroit, Michigan; Dr. Eugene P. Pendergrass, Philadelphia, Pennsylvania; Dr. Leo G. Rigler, Minneapolis, Minnesota; Dr. Charles Sherwood, Rochester, New York.

AMERICAN RADIUM SOCIETY

The Thirty-seventh Annual Meeting of the American Radium Society will be held at the Shoreham Hotel, Washington, D. C., April 21, 22 and 23, 1955, ending the day before the convening of the Fifth Inter-American Congress of Radiology also to be held at the Shoreham Hotel.

FIFTH INTER-AMERICAN CONGRESS OF RADIOLOGY

The Fifth Inter-American Congress of Radiology will be held at the Shoreham Hotel, in Washington, D. C., April 24 through April 29, 1955. This is the first opportunity American radiologists have had to receive and entertain their Latin American friends. It is anticipated that there will be a large attendance.

The Program Committee has well advanced plans for an exceptionally fine program, a prominent feature of which will be refresher courses both in English and in Spanish.

Through the kindness of the United States Public Health Service, there will be a day devoted to a refresher course in the radioactive isotopes followed by a guided tour of the National Cancer Institute and of the National Cancer Hospital.

The fact that the Congress is immediately preceded by the annual meeting of the American Radium Society (April 21–23, 1955) offers an opportunity for a fairly prolonged graduate course which, no doubt, many radiologists, both North American and Latin American, will wish to embrace.

Numerous social events will be included in the program, with special attention to the entertainment of the ladies.

Mark your calendar now for April, 1955, and help to make this the greatest Inter-American Congress held thus far.

TRI-STATE RADIOLOGICAL SOCIETY

A new organization, The Tri-State Radiological Society, has been formed to serve the interest and needs of radiologists in southern Indiana, the northwestern part of Kentucky and the southeastern part of Illinois. The following officers were elected to serve during 1953–1954: *President*, Dr. M. D. FitzGerald, Evansville, Indiana; *Vice-President*, Dr. H. A. Elkins, Mt. Carmel, Illinois; *Secretary-Treasurer*, Dr. S. N. Tager, Evansville, Indiana. Meetings are to be held the last Wednesday of October, January, March and May, at 8:00 P.M. at the Elks' Club in Evansville.

At the last meeting Dr. Alfred I. Sherman of Washington University, St. Louis, Missouri, presented an illustrated lecture on "The Use of Radioactive Gold in the Treatment of Cervical Carcinoma."

WESTCHESTER RADIOLOGICAL SOCIETY

At a recent meeting of the Westchester Radiological Society, the following officers were elected for the coming year: *President*, Dr. Roy D. Duckworth, White Plains, New York; *Vice President*, Dr. Walter Brown; *Secretary-Treasurer*, Dr. Maynard G. Priestman, New Rochelle Hospital, New Rochelle, New York.

ABSTRACTS OF RADIOLOGICAL LITERATURE

Department Editor: T. LEUCUTIA, M.D., Harper Hospital, Detroit 1, Michigan

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ROENTGEN DIAGNOSIS

Head

Beller, Aaron J., and Schwartz, Armin. Pneumoencephalographic studies following complete removal of supratentorial lesions. *Radiology*, Aug., 1953, *61*, 200–207.

Preoperative and postoperative pneumoencephalographic findings in 10 cases of supratentorial lesions are presented and discussed. The purpose of this study was to direct attention to the changes in the ventricular system caused by such lesions, and their reversibility following surgical removal. The cases comprised 5 abscesses, 3 meningiomas, 1 echinococcus cyst, and 1 encapsulated oligodendroglioma.

The most common feature of the postoperative air studies was the return of the displaced ventricular system to its normal midline position. This occurred irrespective of the time interval between onset and date of removal of the lesion. The other constant change after extirpation of the lesion was dilatation of the ventricular system, either symmetrical or asymmetrical. After operation the subarachnoid spaces showed normal filling with some dilatation on the operated side in 9 instances regardless of preoperative filling or nonfilling. The 1 exception showed no filling postoperatively in spite of the presence of air on the preoperative study.

The symmetrical dilatation of the ventricular system following surgery in intracranial, extracerebral lesions such as meningioma indicates that the loss of brain substance is generalized and not local. The asymmetrical dilatation in intracerebral lesions indicates that the loss of brain substance is both general and local; the former due to general increased intracranial pressure, the latter due to local brain destruction. Two cases of brain abscess did not follow this general rule for intracerebral lesions, but the authors feel that this is explained on the basis of too short a time interval between the surgery and postoperative air studies.—*Michael J. Healy, M.D.*

McRoberts, Donald D. Radiological demonstration of the zygomatic arch. *Radiology*, Aug., 1953, *61*, 246–248.

A difficult, though common, technical problem is the adequate demonstration of the zygomatic arch. This prominent facial structure is anatomically composed of the zygomatic process of the temporal bone, posteriorly, and of the malar bone, anteriorly, which is attached to the maxilla on multiple surfaces.

Trauma to this arch usually produces multiple fractures and is often compounded into the maxillary sinus. The fracture details and the particulars of bone displacements are of vital interest to the plastic surgeon, ophthalmologist, rhinologist, and dentist.

Three good routine views are described, along with positioning diagrams and representative roentgenograms illustrating each projection.

(1) The standard nose-chin view for the maxillary sinus is obtained with a cone large enough to include the zygomatic arches laterally. The central ray is directed through the inferior orbital ridges. This shows fractures of the maxillae and antral changes, but the arch is seen only on its superficial convexity.

(2) With the head hanging over the table top in hyperextension, a submentovertex projection is achieved. The chin must be above the central ray and the brow below it. The entire zygomatic arch is visualized clearly, showing all deformities except the up and down plane, which is fairly well seen in the Waters view since the two are practically at right angles.

(3) The usual occipital skull projection with more caudal angulation and with the central ray through the plane of the zygomatic arches, will give an exaggerated view of the arch, plus the temporomandibular joints and often the mandibular condyles as well.

The significant point concerning these projections is that *each view* shows *both* zygomatic arches for comparison, and they are seen at widely different angles for different perspectives in visualization of position and degree of bone disturbance.—*William A. Goodrich, Jr., M.D.*

Monteiro, Hernani, and Ramos, Albano. Metopismo e seios frontais. (Metopism and frontal sinuses.) *Acta iber. radiol. cancerol.*, Jan.–March, 1953, *2*, 57–72.

There is considerable controversy in the literature as to the relationship of unilateral or bilateral agenesis of the frontal sinuses and the presence of a metopic (midline frontal) suture. Thus some investigators believe that congenital absence of one and especially of both frontal sinuses is usually associated with a persistent metopic suture, while others are of the opinion that fully developed frontal sinuses may also be encountered in the presence of a metopic suture.

Professor Amandio Tavares in 1927 made a detailed study of the collection of over 1,000 skulls in the Museum of the Institute of Anatomy of the Faculty of Medicine of Pôrto and found that the incidence of the metopic suture was 10.2 per cent. Professors Roberto Carvalho and Silva Pinto of the same school then, in 1938, published the results of their roentgen investigation on the morphology of the frontal sinuses in 245 skulls, and they stated that bilateral agenesis occurred in 8.3 per cent, while unilateral absence of the frontal sinus was observed in 1.6 per cent on the left side and in 3.2 per cent on the right side.

The authors have now selected from this collection 80 skulls with persistent metopic suture and roentgenographed them to determine the incidence of agenesis of the frontal sinuses. A bilateral agenesis was found in only 6 instances, or 7.5 per cent, and a unilateral agenesis in 2 instances, or 1.25 per cent,

once on the right and once on the left side. These figures closely parallel those of Professors Roberto Carvalho and Silva Pinto which were obtained in an unselected series and thus comprised skulls with and without the presence of the metopic suture.

The authors therefore conclude that metopism does not affect the presence or absence of frontal sinuses. They also state that an intersinusal septum often occurs in the midline and that this finding is of some practical significance in the roentgen differentiation.—*T. Leucutia, M.D.*

WAGGENER, DONALD T., and IRELAND, RALPH L. Intraoral roentgenography for children. *J. Am. Dent. A.*, Aug., 1953, *47*, 133–139.

The authors divide children into several groups for dental studies. In each group different techniques are followed and different sizes and numbers of films are used. This is done in an effort to simplify the examination within the limits of accuracy.

With children from three to six years, due to limited cooperation, the authors recommend a simple method with two small or regular dental films for the posterior teeth. In the case of children between nine and twelve years, twenty films are advised of which eight are of the anterior adult type and twelve standard dental films. They emphasize the use of multiple angle projections to best study the molar regions. In the last group or in those children over twelve years of age, twenty-four films are recommended using variations of kilovoltage according to the different thickness of the regions explored.

The authors content that this simplified method is practical in normal children. When dental abnormalities are found, special techniques and views are, of course, necessary.

The article contains sample roentgenograms made by the various types of examinations and includes photographs of instruments used for obtaining them. A complete chart specifying the examination is also included.—*P. B. Parsons, M.D.*

NECK AND CHEST

BROMBART, M. Le diverticule pharyngo-oesophagien de Zenker; considérations pathogéniques basées sur l'étude radiologique de 26 cas dont 23 au stade de début. (The pharyngoesophageal diverticulum of Zenker; pathogenic evaluations based on the roentgen study of 26 cases of which 23 were in the initial stage.) *J. belge de radiol.*, 1953, *36*, 166–197.

After detailed discussion of the various theories explaining the pathogenesis of this diverticulum, the author agrees with the theory of Holmgren and a few others that this is primarily a pulsion type of diverticulum. The underlying cause is a congenital weakness in the posterior wall of the pharynx at its junction with the esophagus, limited above by oblique fibers of the cricopharyngeal muscle and below by the circular fibers of the same muscle. The latter circular fibers most probably belong to the circular muscle of the upper end of the esophagus.

Four stages of this diverticulum are described, the initial stage being transient and noted only on deglutition or Valsalva's test when there is an increase of the intrapharyngeal pressure. At Stage 1 this diverticulum resembles a rose thorn projecting horizontally from the posterior wall of the pharyngoesophageal junction. The diverticulum is progressive, especially in the male and in many instances it attains the fourth stage in which it exhibits a hanging-sac configuration behind the esophagus beginning most frequently from the level of C-6. In this stage deglutition and other tests do not affect the contraction or the emptying of the diverticulum.

Secondary causes of this diverticulum are: the depression formed in the already congenitally weak and weakening (due to age) musculature of the posterior wall of the lower pharynx on deglutition and the accumulation of food with increased local pressure produced thereby.—*J. N. Sarian, M.D.*

VOSSSCHULTE, K., and STILLER, H. Über die Bedeutung des Pleurahohlraumes bei Störungen und Komplikationen nach Pneumonektomie. (The importance of the pleural cavity in diseases and complications following pneumonectomy.) *Thoraxchirurgie*, Aug., 1953, *1*, 228–244.

The complications of pneumonectomy are listed as follows: (1) Mediastinal and subcutaneous emphysema is common and occurs as early as the first day, postoperatively. Despite tight sutural closure of the bronchial stump, a strong cough may produce such emphysema. It is rarely serious. (2) Emphysema of the contralateral lung occurs especially if bullae are present. The 3 patients who developed this complication died within three days despite all measures. (3) Massive hemorrhage is rare but if suspected requires immediate re-opening of the operative wound. This complication may follow release of extensive adhesions. (4) Infections which are divided into two classes: (a) Primary, or those of unknown origin, despite best aseptic techniques. This type occurred twice in the series of 70 cases. The authors routinely place 10 grams of "marbadal powder" in the thoracic cavity immediately following pneumonectomy; after each thoracentesis, 600,000 units of penicillin and 1 gram of streptomycin are instilled; and on occasions, an additional 100 mg. of aureomycin supplements the other antibiotics. (b) Secondary, or those due to a bronchial fistula. This type occurred in 5 patients in two to seven weeks after surgery. This condition is diagnosed by the usual symptoms of a tension pneumothorax, rapidly increasing dyspnea,

and a persistent negative pressure after thoracentesis. To prevent overwhelming infections, immediate repair is mandatory. A dorsal pleural flap may suffice but a muscle-periosteal flap may be required. The flap is firmly fixed by mattress sutures. The authors strongly advise a simultaneous, extensive thoracoplasty.

With experience and improvement in technique, the authors are no longer concerned with the above, essentially "surgical" complications but are contemplating the fate of the pleural space when the operative wound and the bronchial stump heal satisfactorily. Under these conditions, they have studied the development of a sterile serofibrothorax, elevation of the diaphragm, a shrinkage of the hemithorax on the operated side, and a mediastinal shift to the opposite side. These changes usually proceed slowly, perhaps in six to twelve months. Despite marked mediastinal shift and cardiac displacement, there may be little dyspnea or circulatory embarrassment. Certainly the symptoms do not parallel the roentgenographic picture. Displacement of the great vessels produces few symptoms, if any, whether the pneumonectomy was right- or left-sided. Likewise, tracheal or esophageal displacements are of little moment.

In operating on tuberculous patients, however, the following rules have been adopted: (1) If segmental resection is done, there is no immediate indication for a thoracoplasty. (2) After lobectomy, no thoracoplasty is performed if the remaining portion of the lung expands well enough. (3) After pneumonectomy, thoracoplasty is mandatory, especially if disease is suspected in the contralateral lung.

The authors object to using any foreign body to fill the "dead" space after pneumonectomy. If symptoms arise suggesting a too rapid shifting of the mediastinum, they inject 50–100 cc. of serum without disturbing the existing fibrothorax. If symptoms persist, air but not fluid is withdrawn even if the entire space is filled.

They recommend: (1) Let the "dead" space take care of itself. (2) Avoid a "crippling" thoracoplasty, if possible. (3) Do not use foreign bodies to fill the "dead" space. (4) If negative pressure persists, fill the cavity with serum until a static equilibrium is reached.—*J. Zausner, M.D.*

Weber, H. W., and Löhr, B. Über klinische Befunde und anatomische Veränderungen der Lungen nach Bronchographie mit Per-Abrodil BR (viskös 60%). (Clinical findings and anatomical changes in the lungs after bronchography with per-abrodil BR [viscous 60 per cent].) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Aug., 1953, *79*, 168–179.

Three water-soluble viscous radiopaque substances have been recently introduced for use in bronchography: in Sweden, umbradil-viscose B, in Switzerland ioduron B and in Germany per-abrodil BR (viscous 60 per cent). They are composed of an organic iodine compound and a cellulose derivative which gives the substance its viscosity. The iodine compound is absorbed from the lungs within two to three hours, the cellulose derivative, however, remains in the lumen of the bronchial tree and causes an inflammatory foreign body reaction.

Animal experiments were undertaken with rats, and per-abrodil was introduced through a cannula into the trachea and the bronchial tree. The results of these experiments were considered inconclusive.

Fifteen human operative specimens obtained after bronchography were examined and, in 4, remnants of the cellulose derivative were found to have caused a foreign body reaction with the presence of giant cells and of cells with a foam-like protoplasm. No evidence of diffuse induration of the lungs was observed. This reaction is assumed to be due to filling of the peripleural bronchioli and the alveoli, from where the substance cannot be so easily expelled as from the larger bronchi.

All 4 cases mentioned above showed this type of bronchographic filling.

Acute bronchitis is also considered a cause of defective expulsion of the bronchographic medium and is a contraindication for bronchography. The question of damage to the bronchial mucosa by pontocaine is raised and an interval of a few days between two pontocaine anesthesias is recommended.

In summary, the use of per-abrodil for bronchography is considered safe when peripheral filling is avoided, although the procedure is not entirely harmless and should be used only when indicated.—*Karol E. Matzinger, M.D.*

Boyden, Edward A. Lateral views of the segmental bronchi and related pulmonary vessels in an injected preparation of the lungs. *Radiology*, Aug., 1953, *61*, 183–188.

The segmental bronchi seen on lateral bronchograms are readily identified but little attention has been paid to the identification of the subsegmental rami. These units are the ones which most frequently shift their position on the bronchial tree. The chief pulmonary vessels are even less familiar when seen on lateral projection.

Because of these facts, the author presents several illustrations which show the segmental and subsegmental bronchi on lateral views as well as the chief pulmonary vessels. Supplemental sketches of mediastinal and diaphragmatic surfaces have been added enabling one to comprehend all aspects of a given specimen.

The specimen from which the illustrations were obtained showed three major bronchial variations in each of the lungs and vascular anomalies were still more numerous.—*Donald N. Dysart, M.D.*

Campbell, J. A., and Silver, R. A. Roentgen differentiation of pulmonary tension disorders in infants and children. *Radiology*, Aug., 1953, *61*, 161–173.

Pulmonary encysted or diffuse trapped air under pressure is due to a check-valve mechanism in the bronchial tree, the interstitial substance, or the pleural space. A classification consisting of subdivisions of *congenital* bronchial malformations and of *acquired* interstitial and pleural air cysts is presented. Due to severe respiratory distress, radical surgical intervention is usually required in the congenital types, whereas conservative management is sufficient in most acquired pulmonary tension states. Hence, early differentiation is of critical importance.

Bronchial cysts are the commonest congenital lesions. Focal bronchial dilatation resulting from abnormal growth produces cystic bronchiectasis in the early stage, and if progressive, portions may become pinched off to form cysts. The diffuse form is the congenital honeycombed lung involving the terminal arborization of one or more lobes. In congenital honeycombed lung, there are usually multiple check-valve communications, whereas in cystic bronchiectasis complete patency exists. The cystic hamartoma of lung is seen almost exclusively in premature infants and is composed of an overgrowth of embryonic lung tissue surrounded by tiny alveolar lobules. It contains secretion or air, depending on patency. Sequestration of the lung refers to a segment which separates from the pulmonary tree and has aberrant bronchial drainage and blood supply, the latter often being through the diaphragm.

Most pulmonary tension disorders are acquired. The largest portion is comprised of various forms of regional obstructive emphysema, primarily the postinfectious pneumatocele. This is a check-valve obstruction produced by thick bronchial exudate and edema in a small bronchus supplying an area of interstitial pneumonia, often of staphylococcic origin. Pressure and infection allow rupture of the alveolar septa with formation of large cystic spaces, which may contain fluid levels.

An interstitial bullous cavity is due to weakening of the interstitial elastic tissue, and contains no epithelial lining. The air may dissect along tissue planes and form subpleural blebs, particularly in the apical and diaphragmatic portions. Nontraumatic tension pneumothorax is commonly postinfectious, usually being due to rupture of a suppurative parenchymal lesion or tension cyst in the lung periphery. Previous adhesions may produce a cystiform loculation of the pneumothorax. Diffuse obstructive emphysema is most often a result of an aspirated foreign body or extrabronchial compression. Commonly, progressive expansion of a large part of one lung, lasting two to four days, is followed by atelectasis of the area.

Ancillary facts aiding in the diagnosis of congenital cystic lesions are as follows:

1. Appearance in newborn or neonatal period.
2. Occurrence before a known infection.
3. Growth of lesion commensurate with growth of lung.
4. Absence of collateral inflammation.
5. Trabeculation by septate lung markings.
6. Fluid levels rare.
7. No spontaneous regression in size.
8. Rupture to form tension pneumothorax rare.
9. Fulminating tension states which progress rapidly.

Among *clear cystic rarefactions* solitary congenital cysts and tension pneumothorax produce huge lesions and cause marked rib separation, diphragmatic compression and mediastinal displacement. A large cyst may fill an entire hemithorax but will not herniate across the anterior mediastinum. The congenital cyst compresses the normal lung, and thus the presence of discernible areas of lung tissue at the apex and costophrenic angles with absence of collapsed lung at the hilus typifies congenital cyst and rules against pneumothorax. One also sees irregular trabecular lines crossing the radiolucent area. These represent bronchovascular markings supplying the adjacent lung.

In tension pneumothorax, one sees the clear pleural outline of the collapsed lung even when deformed by pleural adhesions. There is usually a distinct herniation of the pleural sac across the anterior mediastinum. In further differentiation, direct needle aspiration with injection of lipiodol will often demonstrate the confines of a cyst and the extent of the pleural space.

The outline of the interstitial bullous cavity is irregular, thin, and difficult to follow as a continuous line.

Postinfectious pneumatocele is distinguished by the surrounding inflammatory infiltrate and also by serial films showing development from an air bubble appearance, to spherical cavity, to a thin-walled cyst. The pneumatocele may vary greatly from day to day, and usually disappears entirely after several months. Shifting fluid levels frequently come and go, but the lesion is not accompanied by large lobular atelectasis. Unexplained tension pneumothorax may be the initial roentgen finding, due to rupture of the cavity, with other pneumatoceles developing later. In some granulomatous infections (as bronchial tuberculosis) pneumatoceles may develop without a surrounding inflammatory infiltrate. In these, differentiation from a congenital cyst or bullous cavity will depend on changing size, presence of fluid levels, clinical findings and absence of lesion on previous films.

In basal locations, pneumatoceles may resemble emphysematous bullae, diaphragmatic hernia, or sequestration of lung. The latter is characterized by an oval area of increased density in the posterior basilar lung segment with a finger-like extension passing down to the diaphragm. Laminagraphy or

bronchography may suggest solitary cyst or sequestration by demonstrating stenosis or absence of the related bronchus.

In *unilateral diffuse rarefactions*, a congenital cystic hamartoma is suggested by the bronchial mass in the hilus, lack of uniform radiolucency, and the severe mediastinal displacement without hernia, all occurring in a newborn or premature infant. Acquired obstructive emphysema from bronchiectasis or foreign body is often similar.

With *bilateral diffuse rarefactions*, congenital honeycombed lung shows extensive changes in a male infant with few symptoms. The acquired type of honeycombed lung occurs at a later age and shows more interstitial fibrotic density with multiple overlapping small areas of rarefaction. Once infection occurs, the findings are indistinguishable; the cystic cavities become much enlarged, and later interstitial scarring and pleural thickening develop. Bronchography is useful in this first group. In pulmonary emphysema the bronchial pathways are distorted with reduced patency. Cystic bronchiectasis shows numerous tiny cystic cavities in the involved lobes. In honeycombed lung the oil does not enter the cysts, with a resultant distorted pattern in the terminal arborizations.—*William A. Goodrich, Jr., M.D.*

Ames, Wendell R., and Schuck, Miller H. General population roentgenographic surveys: subsequent course of persons considered to have tuberculosis. *Am. Rev. Tuberc.*, July, 1953, *68*, 9–23.

General population roentgenographic surveys, within the limits of the sensitivity and specificity of the screening technique, reveal the amount of illness existing in the population at the time the films were taken and thus give some indication of the prevalence of the disease. They give no indication as to incidence.

"Early diagnosis" is not synonymous with minimal disease and prevalence is far from synonymous with incidence. Analysis of the morbidity and mortality subsequent to original diagnosis is the test of the contribution that mass chest roentgenographic surveys make to the tuberculosis case-finding program.

The Buffalo and Erie County Tuberculosis and Health Association, employing a mobile 70 mm. photofluorographic unit, has been continuously in operation since March 4, 1946, taking 60,000 to 70,000 films per year. The usual procedure is to recall patients with suspected chest disease to a mobile unit follow-up clinic operated by the Association for histories, physical examinations, large chest roentgenograms, tuberculin tests, and sputum examinations when indicated.

This primary follow-up is 86 per cent effective. Of the remaining 14 per cent of the persons examined, two-thirds are successfully followed by the Erie County Health Department after referral from the Association.

This study is based upon the persons diagnosed as having pulmonary tuberculosis who were reported and registered between March 4, 1946 and December 31, 1950. During this period 976 persons were diagnosed as having reportable pulmonary tuberculosis. This is the yield from 330,585 miniature films.

The periods of observation varied from a maximum of somewhat more than five years to a minimum of approximately six months. In tuberculosis, the most rapid change supposedly occurs in the first two or three years of observation. In 47 (45 per cent) of 105 white patients with active minimal tuberculosis followed for less than thirty-one months, the disease remained active at the end of observation. In 17 (25 per cent) of the remaining 68 patients followed for thirty-one to sixty months, the disease remained active. Therefore, 55 per cent of the cases exhibited a change in status within thirty months, but doubling the period of observation yielded only half again as many changes in clinical classification.

Patients were classified into two racial groups, white and non-white, the non-white category being essentially Negro. Among the white patients, three-fourths had no complaints which suggested pulmonary disease. The probability of death from tuberculosis is approximately three times as high among non-whites as among whites.

The bacteriologic findings served to confirm the diagnosis rather than to help in early clinical classification.

Observations made in Erie County and elsewhere indicate that age- and sex-specific tuberculosis mortality rates are now higher among middle-aged and elderly men than among the remainder of the population. Among whites it will be noted that the percentage of persons, classified as having active disease, declines rather uniformly with advancing age. This seems to be true for minimal and advanced disease.

The frequency of progression according to age was quite uniform once the clinical classifications were made.

Six hundred and fifty-six persons were observed for a total of 1,761.2 person-years. During the course of this observation, 23 died from tuberculosis and 10 others died from nontuberculous causes. There were 114 instances of progression of tuberculosis observed.

Persons classified as having active disease were, by and large, younger than those considered to have inactive disease. The natural forces of mortality are considerably less in the younger groups. Therefore, the differences in age distribution of the two groups should not be ignored. Corrected for age, the probability of death was approximately 4.6 times as great among persons diagnosed as having active disease. Among those diagnosed as having disease, but not in the active form, mortality was no greater than in a

comparable age group in the general population.—*Stephen N. Tager, M.D.*

MÜLLER, H. Zystenbildungen in Graphit-Staublungen. (Cyst formation in graphite pneumoconiosis.) *Fortschr. a. d. Geb. d. Röntgenstrahlen ver. m. Röntgenpraxis*, Aug., 1953, *79*, 205–210.

The graphite ores contain a large amount of silicate, and the mining and refining are accompanied by considerable dust formation. This article is based on examination of workers employed in graphite mining, 14 of whom showed definite pneumoconiosis, while 19 others exhibited slight fibrosis of the lungs. The graphite ores with which these workers came into contact contained 3.038 per cent of SiO_2.

Three workers showed roentgen evidence of cavitation. Two of these died and autopsy in one revealed multiple small cavities the size of a bean or hazelnut with smooth walls filled with a thick, black, fat-like liquid containing about 3.5 per cent of carbon. There was no communication visible with a bronchus. The lungs also showed fibrosis, emphysema and multiple fibrous nodules and strands, which were black due to graphite. No tubercle bacilli were found. The cavitation was thought to be due to vascular occlusion by fibrosis. In rare instances, where communication with a bronchus is established, the fluid may be coughed up and an air-containing cavity may be demonstrated on the films. The cysts filled with fluid are, as a rule, undistinguishable from the surrounding dense fibrosis.

The second case developed tuberculosis after suffering from pneumoconiosis for ten years. On autopsy, both tuberculous cavities and graphite containing fluid cavities were found, besides fibrosis and emphysema.—*Karol E. Matzinger, M.D.*

CHARR, ROBERT. Respiratory disorders among welders. *J.A.M.A.*, Aug. 15, 1953, *152*, 1520–1522.

The fumes of welding, particularly those arising from fluorides, cadmium, and chromium used as coating on the electrodes, are stated to be irritating to the respiratory tract. Cough, expectoration, chest pain, sense of oppression about the thorax, and hemoptysis with fever, known as metal fume fever, may develop as an acute reaction. With continued exposure roentgenologic changes are encountered in the lungs, consisting of exaggerated linear markings and nodulation. It is generally believed that the iron dusts, when inhaled into the lungs, are inert. The particles are deposited in the lymphoid tissues and do not cause fibrosis.

The changes on chest roentgenograms are indistinguishable from those of silicosis, but the condition is not crippling as is silicosis. In silicosis the changes are permanent; but in welders, once the exposure is stopped, the disease does not progress and will to some extent regress. Seven case histories are given of welders with respiratory symptoms. In 3 the symptoms were sufficiently severe to necessitate a change of occupation. Two of the patients had tuberculosis as a complication. The clinical course of tuberculosis in welders is considered to be about the same as that in the general population.—*Arthur S. Tucker, M.D.*

ROSENBAUM, HAROLD D., NADAS, ALEXANDER S., and NEUHAUSER, EDWARD B. D. Primary myocardial disease in infancy and childhood. *A.M.A. Am. J. Dis. Child.*, July, 1953, *86*, 28–44.

Rheumatic heart disease and congenital heart disease account for the vast majority of cardiac disorders in infancy and childhood. Within the past few years, a number of patients were seen at the Children's Medical Center, Boston, with severe heart disease of a type which could not be fitted into either of the above two groups. They all had the following features in common: (1) cardiomegaly; (2) absence of significant murmurs; (3) electrocardiographic abnormalities; and (4) normal blood pressure.

The following pathological processes were found in 26 of the patients who came to autopsy: (1) glycogen-storage disease of the heart; (2) aberrant left coronary artery; (3) medial necrosis of the coronary arteries; (4) idiopathic myocarditis, and (5) subendocardial sclerosis.

The patients did not appear to have rheumatic heart disease because of their very early age and the absence of major and minor manifestations of rheumatic fever. Congenital heart disease in the conventional sense (*i.e.*, anomalies of the great vessels, valves and septa) was excluded by the absence of murmurs, abnormal blood pressure, or evidence of shunts in either direction. The clinical picture presented by the group, plus autopsy experience on some of the patients, led to the belief that this syndrome was a primary disease of the myocardium.

The roentgenograms in all patients showed a great similarity as did the clinical features. The heart was enlarged in every instance and usually to a marked or even an extreme degree. The enlargement was generalized, involving all chambers of the heart. Usually the silhouette of the heart was globular in shape. It was not unusual for the heart to touch the left lateral chest wall because of its massive size. In fact, at times, the entire chest was practically filled with the cardiac shadow. This frequently led to pressure upon the bronchi, with resulting poor air exchange and even collapse of portions of the left lung. The absence of a roentgen appearance of increased or decreased pulmonary blood flow was considered very valuable evidence against left-to-right shunts and pulmonic stenosis respectively.

In the paper, the authors attempt to establish

clinical criteria for the differential diagnosis of the five separate diseases causing the cardiac changes in living patients. All of the patients showed, besides the marked cardiomegaly in the roentgenograms, left ventricular hypertrophy in the vast majority of instances and T-wave changes of myocardial damage in the electrocardiogram.

Thirteen of the 19 living patients of the series received digitalis. The response of the majority of the living patients to digitalis was excellent. Only 3 of the 13 patients receiving digitalis did not respond to such therapy but they did improve satisfactorily on mercurial diuretics.—*R. S. Bromer, M.D.*

Williams, Howard, O'Reilly, R. N., and Williams, Alan. Fourteen cases of idiopathic myocarditis in infants and children. *Arch. Dis. Childhood*, Aug., 1953, *28*, 271–283.

The authors present 14 cases histories of patients mainly under two years of age with a diffuse myocarditis for which no cause could be found.

The cases were divided into two groups: (A) the acute type; (B) the subacute, or chronic type.

The acute type was characterized clinically by a sudden onset of severe cardiac failure with respiratory embarrassment, cyanosis, tachycardia with low or normal temperature, an enlarged heart and liver, and electrocardiographic changes of myocardial damage. The illness was commonly mistaken for pneumonia as the respiratory difficulty was the outstanding feature and cardiac enlargement was sometimes impossible to detect clinically, especially in the very young infants. Roentgen examination of the chest usually showed gross uniform cardiac enlargement. The lung fields were often hazy but not congested. Small bilateral pleural effusions were sometimes seen.

Of the 9 patients in this group, 7 had a rapidly fatal illness. The other 2 were diagnosed early and responded to digitalis and oxygen therapy. They recovered completely with no residual cardiac damage.

Postmortem examination in all fatal cases showed widespread but usually patchy muscle damage with inflammatory cell reaction.

The subacute and chronic group included 5 patients who had illnesses of malaise or vague ill health for a month or more before cardiac failure developed. The physical signs present in all cases were cardiac enlargement, tachycardia, gallop rhythm, liver enlargement and, by contrast, minimal signs of pulmonary congestion. The chest roentgenograms showed essentially the same findings as in the acute type: gross but symmetrical cardiac enlargement, hazy lung fields and often small bilateral pleural effusions.

All patients in this group responded to digitalis therapy but relapsed at varying intervals. All have developed permanent cardiac damage.

The authors could offer no clue as to the etiology of the disease.—*Leslie L. Lemak, M.D.*

Palmieri, G. G. Untersuchungen der kardiopneumatischen Phänomene ("Kleine, kardiale Atmung") mit Röntgenkymographie und selektiver Pneumokardiographie. (Investigations of the cardiopulmonary phenomena ["small, cardiac respiration"] with the aid of roentgen kymography and selective pneumocardiography.) *Radiol. clin.*, July, 1953, *22*, 324–334.

Since 1947, the author has performed a series of investigations to determine by means of roentgen kymography the significance of the synchronous movements of the pulmonary structures with the pulse beats of the heart and great vessels. Later, he studied the contrary movement of the apical and basal parts of the lung with the aid of selective pneumocardiography. The findings were published in several papers.

Some objections were raised by other investigators as to the validity of the author's theory of respiration postulated on the basis of these findings. Therefore he, in the present article, sets forth additional documentary evidence in support of his theory and gives a detailed account of the observations made.

He concludes that the heart beat leads to a pulse-synchronous expansion and contraction of the lung parenchyma, which he calls the pulmonary diastole and systole respectively. Thereby the air in the lungs in moved, resulting in the "small or cardiac respiration." The contrary movements of the apical and basal parts of the lungs brought about by the action of the ribs and diaphragm are responsible for the "large respiration." The physiologic or "total respiration" is a combination of the "small, cardiac respiration" and the "large, costodiaphragmatic respiration."—*T. Leucutia, M.D.*

Bruwer, André. Roentgenologic findings in anomalous pulmonary venous connection. *Proc. Staff Meet., Mayo Clin.*, Aug. 26, 1953, *28*, 480–485.

Recent advances in thoracic surgery make it very important to be able to diagnose cardiovascular anomalies accurately. A crescentic saber-shaped shadow of vascular density that runs downward parallel to or behind the right side of the heart and disappears from view in the region of the right cardiophrenic angle usually represents a vein draining the blood from the right lung into the right atrium or inferior vena cava. This is often associated with a shift of the heart into the right half of the thorax which is partly due to an enlargement of the right side of the heart. Another feature often found is a small right hemithorax presumably due to the diminished function of the anomalously drained lung.

Several cases have undergone bronchoscopic and bronchographic examinations and were found to have hypogenesis of one or more bronchi on the right or several of the bronchi ending in blind pouches. Therefore, these examinations should always be done before surgery is attempted. Other features frequently found are a characteristic fullness of the right cardiac border and a small aorta which reflects the diminished volume of blood transmitted.

In cases of total anomalous pulmonary vein connection, in which all the pulmonary venous drainage is into the left heart, a typical figure 8 configuration is found. The pulmonary artery and ramifications are always large and are seen to pulsate vigorously because of the re-circulation of blood through the pulmonary system. Much information can be gained by studying these cases with selective angiocardiography, cardiac catheterization and laminagraphy. It is hoped that more accurate roentgenologic criteria will be established as more cases are uncovered.—*William C. MacCarty, Jr., M.D.*

SLATTERY, R. V. Heart disease discovered on chest microfilms. *J.A.M.A.*, Aug. 22, 1953, *152*, 1595–1596.

The accuracy of chest microfilms in the detection of heart disease was studied in 682 patients. Fifty-six patients had clinical evidence of heart disease and of this number 25 (45 per cent) were detected on the microfilms.

The author describes the methods used in this study and gives a detailed analysis of the results. Thirty-seven patients were thought to have an abnormal heart, but only 25 cases proved to be so on clinical investigation. This is a confirmation rate of 68 per cent which is similar to other reported studies. The tendency to detect a cardiac abnormality on the microfilm coincided roughly with the degree of enlargement of the heart. Thus, rheumatic, hypertensive and arteriosclerotic heart disease were detected most often.

Because of its low degree of detection, the microfilm is not recommended for use in large series for finding persons with heart disease.—*Seymour A. Kaufman, M.D.*

FREER, J. L., and MATHESON, W. J. Left auricular enlargement in endocardial fibroelastosis. *Arch. Dis. Childhood*, Aug., 1953, *28*, 284–287.

Seven cases of endocardial fibro-elastosis are presented. The patients ranged in age from two weeks to six years and all died within two months after the diagnosis was made.

The usefulness of left auricular enlargement as a diagnostic sign is stressed. This enlargement is considered to be present if roentgenograms show: (1) backward displacement of the barium-filled esophagus in the right anterior oblique position; (2) a dense left auricular shadow within the cardiac shadow in the posteroanterior view; and (3) deviation of the barium-filled esophagus to the right in the posteroanterior position.

Fluoroscopy was carried out in 6 patients, with definite left auricular enlargement being present in five.

The other roentgenological features consisted of cardiac enlargement which was predominantly left sided, and pulmonary changes.

Blumberg and Lyon's statement in 1952 that endocardial fibro-elastosis is one of the commonest types of fatal heart disease affecting infants was borne out by this article. The 7 fatal cases described here were seen in a period of eighteen months.—*Leslie L. Lemak, M.D.*

KATZ, BEN E., and ADAMS, FORREST H. Endocardial fibroelastosis; report of unusual case with impaired ability to fabricate serum proteins. *A.M.A. Am. J. Dis. Child.*, Aug., 1953, *86*, 186–197.

Attempts have been made to define endocardial fibroelastosis or endocardial sclerosis as a clinical entity and one which in many cases can be diagnosed antemortem. In this report extensive clinical studies are reported in detail made in a six year old child with endocardial fibroelastosis whose clinical findings differed from the usual.

The postmortem findings of the condition have been described in infants from three days to five years of age, and the majority of deaths have been in infants between four and nine months. In general, three clinical patterns have been noted, characterized best by their course: (1) sudden death occurring twenty-four to forty-eight hours after the onset of symptoms of respiratory distress; (2) prolonged progressive increase in dyspnea, anorexia, irritability, occasional vomiting, cardiac failure and death; (3) repeated episodes of respiratory distress and cardiac failure which respond well to oxygen and digitalis therapy and which may last months or even years.

The unusual features in the case reported were the somewhat atypical physical findings, particularly the persistent edema. After extensive study, it was concluded that the edema was in part due to low plasma proteins, secondary to impaired ability of the liver to fabricate such proteins. Another features was the diffuse enlargement of the heart rather than the commonly observed left-sided changes. The repeated episodes of myocardial failure, usually initiated by an intercurrent infection, shown by the patient, were compatible with the diagnosis of endocardial fibroelastosis.—*R. S. Bromer, M.D.*

MARDER, SUMNER N., SEAMAN, WILLIAM B., and SCOTT, WENDELL G. Roentgenologic

considerations in the diagnosis of congenital tricuspid atresia. *Radiology*, Aug., 1953, *61*, 174–182.

Eight cases of congenital tricuspid atresia are presented. Both conventional roentgenographic studies and angiograms are considered from the standpoint of contributions of both to the diagnosis of this complex malformation.

The most important information to be gained from conventional roentgenograms is provided by a consideration of the caliber of the intrapulmonary branches of the pulmonary artery, since this may reflect blood flow and/or pressure within the pulmonary circulation and, hence, the presence or absence of pulmonic stenosis. Extensive bronchial collateral circulation may somewhat obscure the characteristic clear lung fields in this entity so that number, distribution, and especially caliber of the vascular shadows in the mid-portions of the lung fields must be carefully evaluated. Engorged pulmonary arteries are clear evidence against pulmonic stenosis. Such cases are ordinarily associated with transposition of the great vessels of a high interventricular septal defect. Cardiac contour was not found to be diagnostic, per se. The presence of a right-sided aortic arch, while probably favoring the diagnosis of tetralogy of Fallot, does not exclude the possibility of tricuspid atresia. Deficiency of the lower half of the right heart border in the posteroanterior and left anterior oblique views was thought to be "characteristic" of congenital tricuspid atresia, but if the size of the atrial septal defect is small relative to the size of the mitral orifice, the right auricle may be dilated or hypertrophied. In this event, the lower half of the right cardiac contour is full and the "characteristic" contour is absent.

The angiographic signs are sequential opacification of the right auricle, left auricle and left ventricle. A helpful sign in differentiating this malformation from other cases of single ventricle is the presence of a triangular nonopacified area at the diaphragmatic surface of the heart in the region of the right ventricle. This is best seen in the anteroposterior projection. The usually associated subpulmonic stenosis was not directly visualized in any of the authors' cases. They state that conventional roentgenograms are more reliable in the diagnosis of subpulmonic stenosis from evaluation of reduced caliber of pulmonary vessels.

Formerly, the secondary diagnosis of pulmonic stenosis was more important than that of the basic malformation since these patients might be helped by aortico-pulmonary anastomosis. Now, however, more emphasis is being placed on more complete anatomical diagnoses since in cases with a small interauricular septal defect the patients may be benefited by enlarging the septal defect and forming a systemic pulmonary shunt.—*Michael J. Healy, M.D.*

Nabarro, J. D. N. Cardiac involvement in malignant lymphoma. *A.M.A. Arch. Int. Med.*, Aug., 1953, *92*, 258–264.

Three cases illustrating the misleading clinical nature of lymphomatous cardiac involvement are presented. In the experience of the author lymphomas frequently involve the heart, but symptoms are uncommon, and involvement usually is not suspected ante mortem.

When cardiac signs have been present, they were usually found to be those of pericardial effusion or intractable congestive failure. Such signs may be so prominent that the underlying disease may be overlooked.

The heart may be involved by diffuse infiltration or invasion of the lymphoma from the mediastinum. In cases with effusion, examination of the pericardial fluid may reveal characteristic cells.

The usual treatment of the failing heart, or pericardial aspiration, where indicated, has been found disappointing. A brief remission has been achieved in a few instances with deep roentgen therapy of the heart.—*Thomas B. Efford, M.D.*

Benchimol, Aaron Burlamaqui, and Schlesinger, Paul. Beriberi heart disease. *Am. Heart J.*, Aug., 1953, *46*, 245–263.

Beriberi heart disease is not uncommon in Brazil. In a three year period a series of 22 patients with the disease syndrome have been identified by the authors. As has been previously pointed out by Weiss and Wilkins, the clinical picture of cardiac beriberi in the Western Hemisphere frequently differs considerably from the classical syndrome originally described in the Orient. Thus, right-sided heart failure was not in the presently reported cases a common occurrence as an isolated finding, but was usually associated with signs and symptoms of left ventricular insufficiency such as dyspnea, orthopnea, and cardiac asthma. Furthermore, the frequent absence of the hyperkinetic circulatory syndrome, which is considered so highly characteristic of beriberi heart disease in the Orient, deprives the physician of one of the important diagnostic features of this condition. Under these circumstances it is not surprising that such cases are often misleading, since they so closely resemble other more common types of degenerative heart disease.

Most cases of beriberi in the Occident occur as a result of chronic alcoholism. The excessive intake of alcohol predisposes to beriberi by inducing thiamin deficiency which is the primary factor in this condition.

The cases reported were all males, in the 30–40 age group, engaged in employment requiring great physical exertion, Clinically, the patients mainly presented themselves with dependent edema and dyspnea as initial symptoms; pulmonary congestion

was found on physical and roentgenologic examination, confirming the impression that right- and left-sided heart failure occur concomitantly in the Western form of the disease. Ten of the 22 patients showed signs of rapid circulation as judged by circulation times; however, only 5 of these had typical hyperkinetic circulatory syndromes with increased pulse pressure, bounding pulse, a normal circulation time in the presence of congestive failure, and increased cardiac pulsations on fluoroscopic examination.

The authors conclude that although the clinical manifestations are usually sufficient to suggest the diagnosis of beriberi heart disease, particularly if the patient is a chronic alcoholic, it is evident that the roentgenologic and electrocardiographic changes, as well as the therapeutic effects of thiamin, are far more significant diagnostic features of the disease.

The roentgenologic findings in cardiac beriberi are usually not typical, although a reduction in heart size following a favorable response to thiamin therapy is included as an important feature of the condition.—*Harold Fulton, M.D.*

Abdomen

Seedorf, E. E., Powell, W. N., Greenlee, R. G., and Dysart, D. N. Telepaque and pseudoalbuminuria. *J.A.M.A.*, Aug. 1, 1953, *152*, 1332–1333.

The authors studied 100 patients who had received (3-[3-amino-2,4,6-triiodophenyl]-2 ethyl propanoic acid) (telepaque) for the performance of cholecystography and compared this with a group of patients who had been given iodoalphionic acid (priodax) and with another group of patients who had received (2-[4-hydroxy-3,5 diiodobenzyl] cyclohexane carboxylic acid) (monophen). It was found that pseudoalbuminuria, as determined by the hot Exton's reagent test, was caused by all three media in about 15 per cent of the patients. Side reactions and their frequency were relatively the same with all three materials.

All three media produced satisfactory cholecystograms. An undesirable result of the use of telepaque is a residual deposit in the bowel which can cause interference with the interpretation of calculi.—*Frank J. Rigos, M.D.*

da Silva, Martins. Progressos na vizualização radiólogica das vias biliares. (Progress in the radiologic visualization of the biliary pathways.) *Acta iber. radiol. cancerol.*, Jan.–March, 1953, *2*, 29–56.

The author reviews the various opaque media used in cholecystography since 1924, when Graham and Cole originated the method. The latest in the series is telepaque which was introduced in 1951 and which consists of 3-(3-amino-2,4,6-triiodophenyl)-2-ethyl-propanoic acid containing 66.68 per cent iodine in organic combination.

He personally tried this new medium in 16 patients and obtained very satisfactory results. The mode of administration of the drug, the technique of the roentgen examination and the advantages over other similar drugs are discussed in detail. The 16 cases are tabulated and their histories are presented.

The conclusion is reached that telepaque produces opacification of an increased density with an increased percentage of visualization as compared to other media, requires fewer hours for maximum concentration and often renders visible the extrahepatic biliary pathways thus permitting a diagnosis of lesions of the cystic canal and of the common bile duct.—*T. Leucutia, M.D.*

Bell, Luther G., Brown, Robert B., and Lenhardt, Harry F. Acute pneumocholecystitis; a review and report of two cases. *Ann. Surg.*, Aug., 1953, *138*, 268–274.

The authors reviewed 25 cases of acute pneumocholecystitis reported between 1908 and 1949 and have added 2 of their own.

Gas may be found in the gallbladder due to the following factors: (1) fistulous communications between the gallbladder and gastrointestinal tract; (2) reflux through a patent sphincter of Oddi; and (3) bacterial action secondary to mechanical, vascular or toxic changes in the organ. Diabetes was an apparent predisposing factor in 8 (30 per cent) of the reported cases. The 2 cases reported by the authors fit into the third category and were not associated with diabetes.

The clinical picture seen in this disease is similar to that of acute cholecystitis. The diagnosis is made on roentgen evidence of gas within the gallbladder. This must be differentiated from lipomatosis, which maintains a static configuration.

The authors believe the treatment of choice is surgery. Their 2 cases had cholecystostomy together with antibiotic and supportive therapy. Treatment in the past has ranged from conservative medical management to cholecystectomy.—*Geno DiBagno, M.D.*

Simon, George, and du Boulay, George. The value of radiology in assessing the progress of duodenal ulceration under treatment. *Proc. Roy. Soc. Med.*, Aug., 1953, *46*, 655–662.

One hundred and thirty-four consecutive cases of duodenal ulcer were examined by the authors; an ulcer crater was seen with reasonable certainty in 63, all of which showed some cap deformity as well. Many of these were re-examined after intervals varying between a few weeks and two years during which they had been treated medically. In most instances the ulcer crater became smaller as pain subsided.

Frequently the crater was still present though the pain had completely remitted. It is argued that while symptoms are still present re-examination by barium meal is unnecessary, and after symptoms have disappeared roentgen "control" of treatment is of no value in the majority of cases.

Seventy-one of the patients showed duodenal cap deformity only; the roentgen appearance remained unchanged in the great majority of cases regardless of the symptoms. No examination took place after intervals of from a few weeks to three years.

It is concluded that roentgenologic examination has little to offer which will help the clinician in deciding how effective treatment has been or what further treatment should be instituted. Recurrence of similar symptoms is not an indication for re-examination, providing the original diagnosis is not in doubt and that good roentgenograms were taken on a previous occasion and are available for inspection. If the character of the symptoms changes, suggesting, for instances, obstruction or malignancy, re-examination is, of course, indicated.—*James J. McCort, M.D.*

Lust, Franz J. Correlation of roentgenological studies with certain clinical symptoms in peptic ulcer. *Am. J. Digest. Dis.*, Aug., 1953, *20*, 221–226.

The author attempts to correlate the clinical symptoms with the roentgenologic findings in patients with peptic ulcer. The main complaints in duodenal ulcer are: (1) localized pain; (2) sour somach and heartburn; (3) cramps; (4) fullness; (5) nausea and vomiting, and (6) constipation.

Pain in a peptic ulcer is localized and indicates activity of the process. Careful examination by the fluoroscopist and adequate spot films study will often reveal the ulcer deformity to correspond to the area of localized tenderness. A deformed cap with tenderness over the stomach should lead one to look for a gastric ulcer as the deformity may be due to fibrosis.

Sour stomach and heartburn are represented by the increased amount of secretion found in the stomach. Mucus does not mix easily with barium and is visualized as a "mottling" overlying the gastric mucosa. Hypersecretion of the stomach in ulcer cases is thus demonstrated on the films, giving the examiner some indication of the secretory function. Mucosal studies frequently show broad, tortuous rugae which have increased turgor.

Epigastric cramps are mostly due to spasm of the pylorus. These present themselves on the film as an increased distance between the cap and the antrum.

Fullness is generally due to delayed emptying of the stomach. The terminal stage of the pyloric pathology in peptic ulcer is fibrosis. With an advanced degree of organic pyloric stenosis, the findings are those of large atonic stomach with a large twenty-four hour residue. The vomiting in this case must be treated surgically.

The roentgenological equivalent of constipation, a very distressing symptom, is found on the twenty-four hour examinagion. There is apparently increased reabsorption of fluid in the colon which dries out the stools or barium. The barium column is broken off into several round or oval-shaped masses casting a very dense shadow and is irregularly distributed throughout the colon.—*Seymour A. Kaufman, M.D.*

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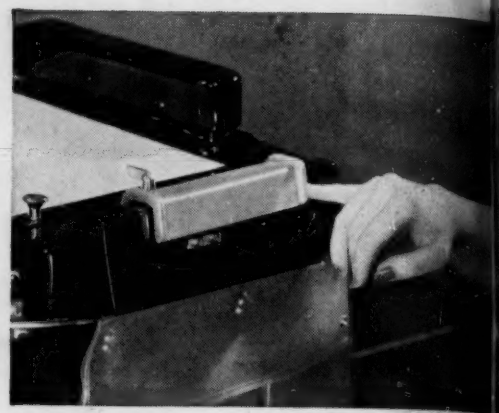
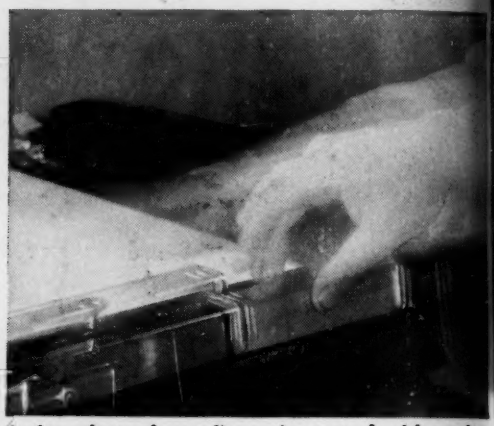
Photo shows fingertip control of screen and tower. Easy movement provides efficient and effortless operation for the radiologist.



Fingertip pressure unlocks and moves screen in one motion.



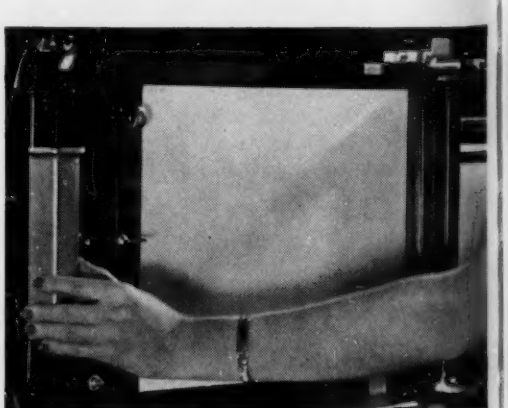
Action photo shows fingertip control with motion stopping smoothly.

MOVES AT A TOUCH

The Westinghouse Power Assist now takes all extraneous effort out of fluoroscopy. In any position of the table, the device adds thrust to the doctor's fingertips so that screen and tower glide easily along the table, or up and down when table is vertical.

The control is mounted on the forward edge of the screen, operates with locks off or on. When pressed longitudinally or vertically, it releases the proper locks and moves the screen; when the pressure is released, the magnetic locks engage and motion stops smoothly.

For information on further advantages of this newest advance in fluoroscopy, ask your Westinghouse representative for details. Or write the address below, Dept. A-86 for further information.



In the vertical position, the same ease of operation is achieved.

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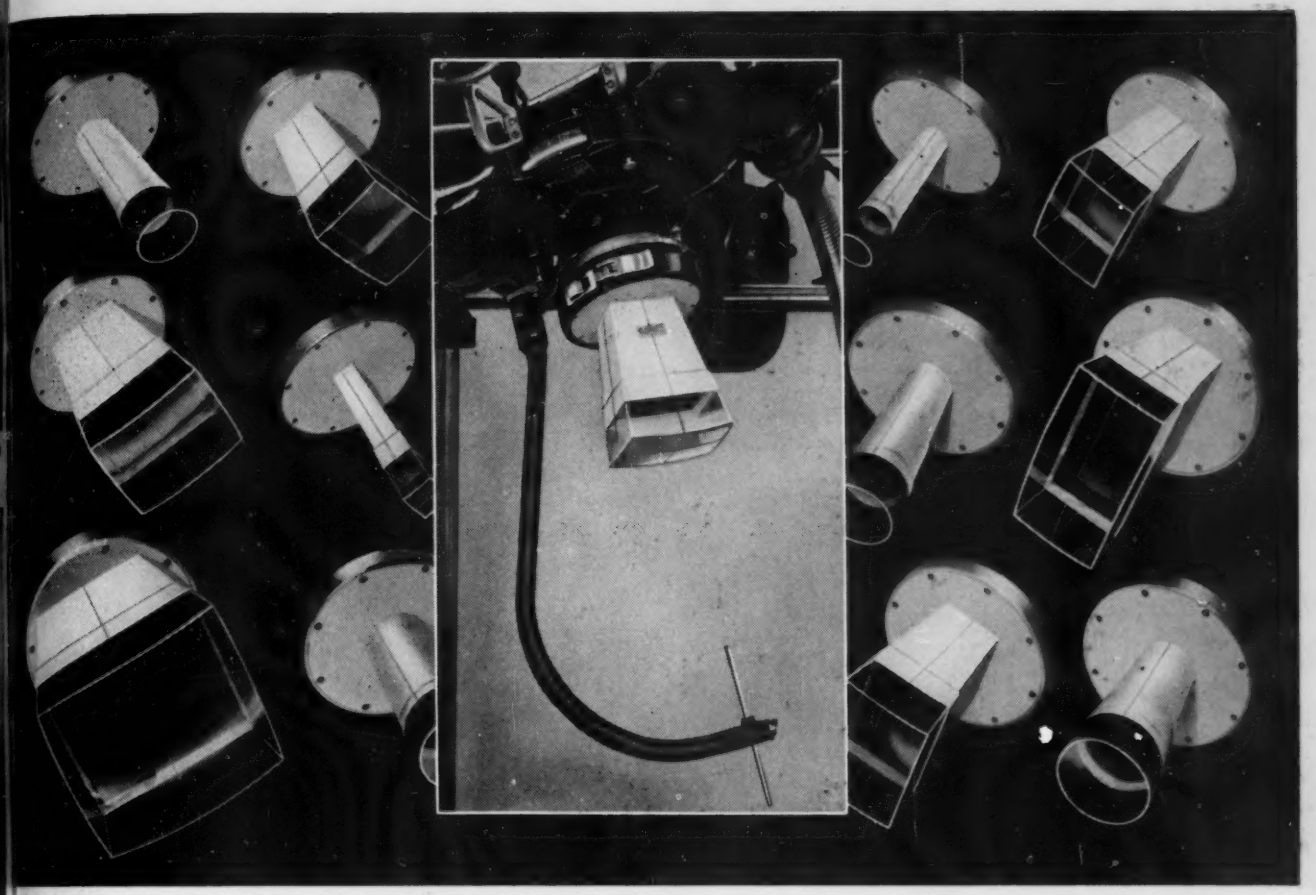

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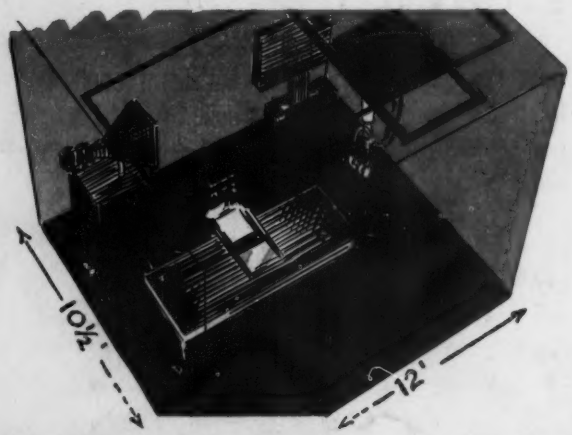
can you quickly center x-ray beam—to body part—to Bucky without having to match up separate scales for tube position and table position?

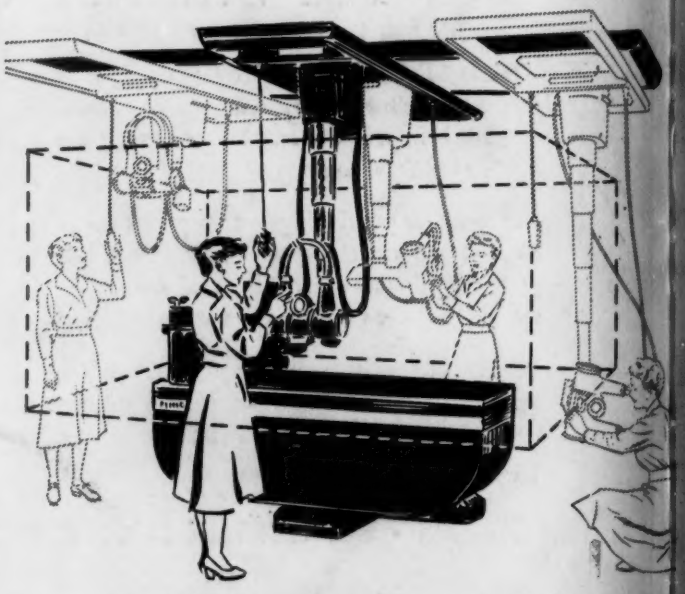
can you do lateral radiography from the front, or from either end, or from the rear of the table?

can you (or a group) stand or work *anywhere* around the full circuit of the table... front, back, head or foot?

can you radiograph a stretcher case in front, or at either end, or behind the table without hindrance... *and without having to shift the table?*



can you place pieces of auxiliary apparatus *anywhere* in the room with plenty of floor space to run a stretcher up to, and work easily at them?



can you do all this in a room only 10½' x 12'? (the girls spotted around the table show how easily you can position the x-ray tube anywhere within the dotted-lines)

you get through *more work faster*
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